STUDIES IN THE REDUCTION OF KETONES

PART I - PROMOTION OF THE HYDROGENATION OF KETONES OVER RANEY NICKEL CATALYST.

PART II - THE STEREOCHEMISTRY OF THE CATALYTIC REDUCTION OF KETONES.

A Thesis submitted for the
DEGREE OF DOCTOR OF PHILOSOPHY
at Glasgow University

by

ROBERT BRUCE BLANCE, B.Sc.

March, 1957.

PART I.

PROMOTION OF THE HYDROGENATION OF KETONES OVER RANEY NICKEL CATALYST.

INDEX TO PART I

Experimental (Contd.) Page

S U M M A R Y

Various methods of promoting Raney Nickel in hydrogenation reactions have been described in the literature. Confining attention to the reduction of the carbonyl group, these methods have been compared and a more effective method of promotion has been developed in which the catalyst is platinised with a triethylamine chloroplatinic acid complex and then treated with sodium hydroxide. Experimental observations indicate that the action of sodium hydroxide in the promotion of the hydrogenation may be interpreted as overcoming a retardation caused by the alcoholic products of the reaction.

I N T R O D U C T I O N

A prerequisite of chemical reaction at a surface is the adsorption of the reacting species. Two types of adsorption occur (1):-

(a) physical adsorption which is relatively weak; the forces corresponding to those assumed in the Van der Waal's equation of state of gases, play only a minor part in connection with surface reactions since they are not sufficiently strong to influence appreciably the reactivity of the adsorbed molecules.

(b) chemisorption which is associated with the formation of valence bonds between the surface and the adsorbed molecule. In surface reactions at least one of the reacting species must be chemisorbed.

The formation of valence bonds is affected by two properties of the catalyst:- (a) the geometry of its surface and (b) its electronic configuration (2). The effect of the geometry of the surface was shown in the hydrogenation of ethylene using oriented nickel films which expose the 110 planes preferentially. Such films were found to be five times more active than non-oriented films (3). The electronic factor is, however, the more important since

reaction can occur when the geometric factor is unfavourable, e.g. the hydrogenation of benzene occurs on iron films to produce cyclohexane while metals such as silver and cadmium with a favourable geometric factor for this reaction are inactive.

Dowden (4,5), and Dilke, Maxted and Eley (6), have suggested that the high catalytic activity of the transition metals could be explained if chemisorption involved the metal d-band. Non-transition metals would be relatively inactive because there are no d-band vacancies through which covalency could take place. A number of investigations have produced evidence for this (7,8,9). Dowden (5), in a theoretical treatment suggests that the real bonds formed in chemisorption are intermediate between the two extreme types of ionic and covalent bonds. In ionic binding a transfer of electrons to or from the metal catalyst yields a substrate ion held to the surface by image forces. Covalent binding is regarded as a donation of electrons to the unfilled d-orbitals of the metal surface. The activity of the catalyst is related by him to the electron exit work function. When the rate-controlling step of a catalytic reaction involves donation of an electron to the catalyst then in a series of catalysts the activity increases with increasing electron exit work function. The activity

increases with decreasing work function when the rate-controlling step involves transfer of an electron from the surface. Experimental confirmation of his theories was obtained (8). Dowden suggests that addition of strongly electropositive substances to a catalyst, by lowering the work function, poisons reactions which proceed via a positive ion at the slowest step and promotes reactions which proceed via a negative ion. The effect is reversed with electronegative additives. Beyond a certain range of work function, surfaces which catalyse reactions involving covalently bonded intermediates will be poisoned by electropositive and electronegative contaminants.

Moore and Selwood (9), have shown that changes in the specific magnetisation of nickel occur simultaneously with chemisorption due to a change in the density of unpaired electrons in the d-band. When hydrogen was chemisorbed by a nickel-silica catalyst, the specific magnetisation decreased indicating that electron transfer from hydrogen to nickel occurred. They suggest that the equilibria for hydrogen adsorbed on nickel may be represented thus:-

$$2H^- \rightleftharpoons \underset{\Downarrow H_2}{2H^0} \rightleftharpoons 2H^+$$

, the direction of transfer of electrons depending on the particle size of the catalyst. The decrease in magnetisation normally observed on chemi-

sorption of hydrogen may be caused by the formation of some protons as hydrogen atoms donate their electrons to the nickel surface or as the electrons of the covalent Ni-H bond are more strongly attracted to the nickel atom. But since individual nickel atoms are electron donors and very small particles resemble the individual atom, a new mechanism may operate for these small particles. They may tend to hold electrons more loosely than does hydrogen and in an extreme case a hydride ion may be formed.

For a considerable time there has been controversy about the existence of "active sites" on a catalyst surface. These sites were postulated by Taylor (10), to explain the sintering of catalysts, the effect of small amounts of poison, and the variation of the heat of adsorption with surface coverage. The work of Maxted (11), on the poisoning of platinum catalysts, a theoretical treatment of his results by Herington and Rideal (12), and the studies of Beeck et al. (3), on the properties of evaporated metal films suggested, however, that catalytic phenomena might be interpreted in terms of the properties of a set of uniform sites on plane faces of crystalline materials. Boudart (13), has now explained the phenomenon of "active centres" by suggesting that when adsorption on a uniform surface occurs, a double layer is set up which modifies the electron exit work

function so that there is a fall in the heat of adsorption with surface coverage. Experimental evidence of the change in work function with adsorption has been obtained by Baker and Rideal (14). Boudart considers that heterogeneity is induced on a clean surface by adsorption of reactants, products, poisons and promoters which radically modify the adsorbing properties of the original bare surface. The surface thus acquires optimum or active sites for a particular reaction. Catalysis by a conducting surface is therefore a co-operative phenomenon involving the whole surface even if only a small fraction of it is active at any time.

As yet there are no generally accepted reaction mechanisms in heterogeneous catalysis. One of the most widely studied reactions is the hydrogenation of ethylene. It is generally assumed that chemisorption of ethylene on the surface of transition metals occurs by an associative mechanism in which the double bond is opened and two carbon-metal bonds are formed (15). This may be represented in the following way:-

$$C_2H_4(g) \longrightarrow {}^{*}CH_2\text{-}{}^{*}CH_2,$$

the asterisks indicating the bonds to the metal. The addition of hydrogen to ethylene has been shown to proceed in two stages, the first of which is the production of the "half-hydrogenated state" which in this case is an adsorbed

ethyl radical (16,17). Since the para-hydrogen conversion over nickel is inhibited by the presence of ethylene (18), indicating that the concentration of adsorbed hydrogen is very small, Twigg and Rideal (19), suggested the following mechanism of hydrogenation over nickel catalyst:-

$$H_2C^{*} - CH_2^{*} + H_2 \longrightarrow CH_2 - CH_2^{*} + H^{*} \longrightarrow H_3C-CH_3$$

in which chemisorbed ethylene reacts with physically adsorbed hydrogen. Later Twigg (17), suggested that the adsorbed hydrogen atom formed in the first stage of this reaction undergoes rapid reaction with another chemisorbed ethylene molecule, the net result being:-

$$2\ H_2C^{*} - CH_2^{*} + H_2 \longrightarrow 2\ H_3C - CH_2^{*}$$

$$2\ H_3C - CH_2^{*} + H_2 \longrightarrow 2\ CH_3 - CH_3$$

Recently Jenkins and Rideal (20), have presented evidence which indicates that "associative adsorption" of ethylene does not occur on a nickel surface; on the contrary ethylene on chemisorption is dissociated to an acetylenic complex and chemisorbed hydrogen. The final structure on admission of the two gases to a nickel surface is some 80% coverage by acetylenic complexes, 10% by chemisorbed hydrogen (i.e. hydrogen atoms) and 10% by molecular hydrogen. Sub-

sequent hydrogenation of ethylene proceeds by reaction of gaseous ethylene with chemisorbed hydrogen, i.e., $C_2H_4 + 2H^{\ast} \longrightarrow C_2H_6$. Such a mechanism, however, does not account for the inhibition of the p-hydrogen conversion. Bond (73), in a more recent study of the deuteration of ethylene over various types of platinum catalyst, has interpreted the results in terms of the associative mechanism of adsorption of ethylene. Flanagan and Rabinovitch (74), studying isomerisation and exchange reactions of trans-ethylene-d_2 over a nickel catalyst, found that mechanisms which proceed via an adsorbed ethyl radical, were consistent with their experimental results but they were unable to distinguish the validity of the associative mechanism from that of the Jenkins-Rideal mechanism.

Little is known about the mechanism of catalytic hydrogenation of carbonyl compounds apart from the fact that at room temperature the reaction occurs by addition of hydrogen to the keto form while at elevated temperatures the addition is mainly to the enol form. Evidence for this was obtained by Farkas and Farkas (21), in a study of the hydrogenation of acetone and isopropyl alcohol on platinised platinum foil; by Anderson and MacNaughton (22), in a study of the deuteration of carbonyl compounds over Adams' platinum oxide catalyst, Raney Nickel and copper chromite; and by Freedman

and Turkevich (23), who investigated the catalytic reduction of acetone with deuterium over iron promoted platinum on charcoal and over Adams' platinum oxide catalyst.

In the hydrogenation of carbonyl compounds, Raney Nickel catalyst is frequently used. The catalyst is prepared by leaching aluminium from a Ni-Al alloy with sodium hydroxide. Since its discovery (24), methods of preparing the catalyst of various grades of activity have been published (25,26,27). The catalyst is active in the hydrogenation of alkyne and alkene linkages, aldehydes and ketones, nitro compounds, nitrites, oximes, and benzenoid and pyrinoid nuclei (27). It has been used in oxidation-reduction reactions (28,29), and for dehalogenation (30), and desulphuration (31), of organic compounds.

Taylor and Weiss (32), have shown by X-ray examination that the leaching of aluminum from the Ni-Al alloy creates defect lattices of nickel which possess a very large, highly unsaturated surface at which electron transfer processes should be considerably enhanced. Ipatieff and Pines (33), suggested from analysis of the catalyst that the residual aluminium is present as the oxide and that Raney Nickel is essentially a nickel catalyst promoted by alumina. Watt and Parker (34), however, showed that most of the residual aluminium of the catalyst is in the metallic state, as had

been indicated by Taylor and Weiss. Smith et al (35), found that the hydrogen content of the catalyst varied between one half and one atom of hydrogen per atom of nickel and that the activity was proportional to the hydrogen content, the surface area decreasing with loss of hydrogen. They put forward the concept that Raney Nickel catalyst is a form of nickel promoted with adsorbed hydrogen. Freĭdlin and Ziminova (36), found that the amount of hydrogen adsorbed on Raney Nickel was approximately 100 ml./g. and that only with removal of the last 1-2 ml. did the activity of the catalyst vanish. The ageing of Raney Nickel which has been associated with the loss of hydrogen, is attributed by Pattison and Degering (37), to reaction of adsorbed hydrogen with oxygen to form water, or to the displacement of hydrogen from the surface by the reaction of oxygen with the nickel catalyst.

In hydrogenation reactions, Raney Nickel catalyst has been promoted by various additives of which platinum and certain bases have been found to be particularly effective. In the hydrogenation of ketones, Delépine and Horeau (38), promoted the catalyst by addition of platinum (via a solution of sodium chloroplatinate) and sodium hydroxide. Other noble metals, namely Pd, Ru, Rh, Os and Ir, were effective. Lieber et al (39), in a study of the hydrogenation of carbonyl compounds and aromatic nitro compounds obtained promotion

for nitro compounds and retardation for carbonyl compounds by the addition of platinic chloride to Raney Nickel, and promotion for carbonyl compounds and retardation for nitro compounds by the addition of sodium hydroxide. Paty (40), successfully applied promotion with sodium hydroxide to cyano-, nitro-, and ethylenic derivatives. Décombe (42), found that difficult reductions were achieved readily with platinised Raney Nickel.

The effect that promotion by sodium hydroxide could have on the product of hydrogenation was shown by Fluchaire and Chambret (41). They obtained $PhCh_2CH_2NH_2$ in 51% yield and $(PhCH_2CH_2)_2NH$ in 38% yield in the reduction of $PhCH_2CN$ with Raney Nickel. Promotion of the catalyst with sodium hydroxide yielded 90% of $PhCh_2CH_2NH_2$.

In 1946, Heilmann et al (43), compared the promotion methods of Lieber and of Delépine and found that the Delépine method was more effective in the hydrogenation of nitroguanidine, methyl ethyl ketone and a large number of unspecified ketones. In 1949, J. W. Skelly (44), using Adkins' W-4 Raney Nickel catalyst (26), confirmed the superiority of the Delépine method in the hydrogenation of methyl ethyl ketone. The work reported in this thesis has its origin in Skelly's report.

When Adkins and Billica (27), demonstrated that tri-

ethylamine is an effective promoter of Raney Nickel catalyst, Lieber et al. (45), successfully combined the effects of platinic chloride and triethylamine in the hydrogenation of nitrocompounds, nitriles, aldehydes and ketones over Raney Nickel. They claimed that this method of promotion is the most efficient available.

An extensive study of the hydrogenation of nitro compounds using Raney Nickel treated with chloroplatinic acid and alkali has been published by Samuelson et al. (46). Their results indicated that platinum acts as a true promoter while except for a number of nitro-alkanes addition of alkali retards the hydrogenation.

In this first section of this thesis, a systematic study of the promotion of Raney Nickel in the catalytic hydrogenation of ketones is reported with work designed to give some insight into the mechanism of such promotion.

G E N E R A L

Preparation of Materials.

Except for the cyclopentanones, all the ketones used in the study of the promotion of Raney Nickel were obtained commercially. They were treated with Raney Nickel catalyst prior to distillation in order to remove catalyst poisons. Cyclopentanone was prepared by pyrolysis of adipic acid; ± 3-methylcyclopentanone was prepared by oxidation of 4-methylcyclohexanol to ± β-methyladipic acid which was then pyrolysed to the cyclic ketone; ± 2-methylcyclopentanone was prepared by reaction of methyl iodide with 2-sodiocarbethoxy-cyclopentanone (from diethyl adipate by the Dieckmann reaction), followed by hydrolysis; 2:2-dimethylcyclopentanone was prepared by reacting methyl iodide with ± 2-methylcyclopentanone in the presence of sodamide.

The Raney Nickel catalyst used in the promotion studies was of "W-4" grade, (26), prepared by rapid leaching of nickel-aluminium alloy at 50°.

Preliminary experiments on the hydrogenation of acetone and methyl ethyl ketone over Raney Nickel catalyst.

Preliminary experiments were undertaken in order:-

(a) to find a suitable hydrogenation solvent;

(b) to find promoters of the hydrogenation;

(c) to establish the variables in the reaction.

Hydrogenations were effected at atmospheric pressure, the rate of hydrogen uptake being followed with a gas burette: and at 45 p.s.i. differential pressure the rate of fall in pressure being followed with a Bourdon gauge.

A study of the rate of hydrogenation of acetone in the following solvents - methanol, ethanol, water and dioxan - indicated that the fastest rate of hydrogenation was obtained with methanol and ethanol. Moreover these two solvents gave the best promotion effect when sodium hydroxide was added, while retardation was obtained when sodium hydroxide was added to the hydrogenation system with dioxan as solvent (experimental p. 43).

Traces of oxygen added to the hydrogenation system of Raney Nickel, acetone and ethanol resulted in a retardation of hydrogenation (experimental p. 44).

The rates of hydrogenation at atmospheric pressure and at 45 p.s.i. differential pressure were found to vary directly with the amount of catalyst in the range 0.5 g. - 3.0 g. (experimental p. 45,47); the time of hydrogenation was found to decrease with increase in the initial hydrogen pressure; the rate of hydrogenation was found to be independent of the initial hydrogen pressure over the range 20 - 45 p.s.i. differential pressure (experimental p. 48).

A study of the ageing of Raney Nickel showed that there

was a considerable decrease in the activity of the catalyst with time (experimental p. 48). Addition of sodium hydroxide to the catalyst was found to overcome the ageing effect to a considerable extent since the loss in activity of the promoted catalyst was appreciably smaller.

The promotion effect of certain organic bases was investigated using Raney Nickel and platinised Raney Nickel (experimental p. 50). It was found that trimethylamine and triethylamine promoted the hydrogenation of methyl ethyl ketone while triethanolamine, morpholine and tribenzylamine retarded the reaction. Tetraethyl ammonium hydroxide gave a promotion effect almost equivalent to that of sodium hydroxide. Trimethyl benzyl ammonium hydroxide caused retardation of the reaction which was found to be due to hydrogenolysis of the hydroxide to toluene and trimethylamine, retardation being caused by the toluene (experimental p. 51). Similarly N-methylpyridinium hydroxide was hydrogenated to a high-boiling base which was probably 1:1^1-dimethyl-4:4^1-dipiperidyl (experimental p. 53).

Promotion of the hydrogenation of ketones over Raney Nickel catalyst.

In comparing various methods of promotion of Raney Nickel in the hydrogenation of ketones at atmospheric pressure, the standard scheme adopted was the determination of the time of hydrogenation of 0.01 g. mole. of ketone in ethanol over

0.5 g. of Raney Nickel. The catalyst systems studied were:-

(a) Raney Nickel.

(b) Raney Nickel + sodium hydroxide.

(c) Raney Nickel + triethylamine.

(d) Platinised Raney Nickel + sodium hydroxide (Delépine's technique (38)).

(e) Platinised Raney Nickel + sodium hydroxide + triethylamine.

(f) Raney Nickel + triethylamine + chloroplatinic acid, (Lieber's technique (45)).

(g) Raney Nickel + triethylamine + chloroplatinic acid + sodium hydroxide.

The systems (a), (d), (f) and (g) were also studied in hydrogenations at 45 p.s.i. differential hydrogen pressure using 3 g. of catalyst and 0.05 g. mole. of ketone.

The theoretical amount of hydrogen was taken up in almost every case; the exceptions are given in the tables which follow. In no case investigated did reaction occur at 45 p.s.i. hydrogen pressure and not at atmospheric pressure. However, the elevated pressure enabled the reaction to proceed to completion in a much shorter time as was particularly noticeable with the higher ketones. In every case the product of hydrogenation was the corresponding alcohol. The aromatic ketones were not hydrogenolysed to the hydrocarbon.

Because of the ageing effect on the catalytic activity of Raney Nickel (page 14), all hydrogenations were carried

out within a time interval of three to ten days after preparation of a batch of catalyst, and whenever possible all comparative experiments on the activity of the various promoted catalysts in the hydrogenation of a particular ketone, were carried out on the same day. The hydrogenations were done in duplicate and the times of hydrogenation were reproducible to within 5%. The promotion of Raney Nickel was studied in the hydrogenation of a series of aliphatic, aromatic and alicyclic ketones.

Aliphatic Ketones.

(a) Hydrogenation at atmospheric hydrogen pressure.

The times (in minutes) of hydrogenation of 0.01 g. mole of ketone over the various promoted catalysts are given in Table 1 and the course of hydrogenation is illustrated in Figures 1a - 1c for acetone, methyl isobutyl ketone and diisopropylketone.

FIGURE 1.

HYDROGENATION OF ALIPHATIC KETONES AT ATMOSPHERIC PRES

FIG. 1.

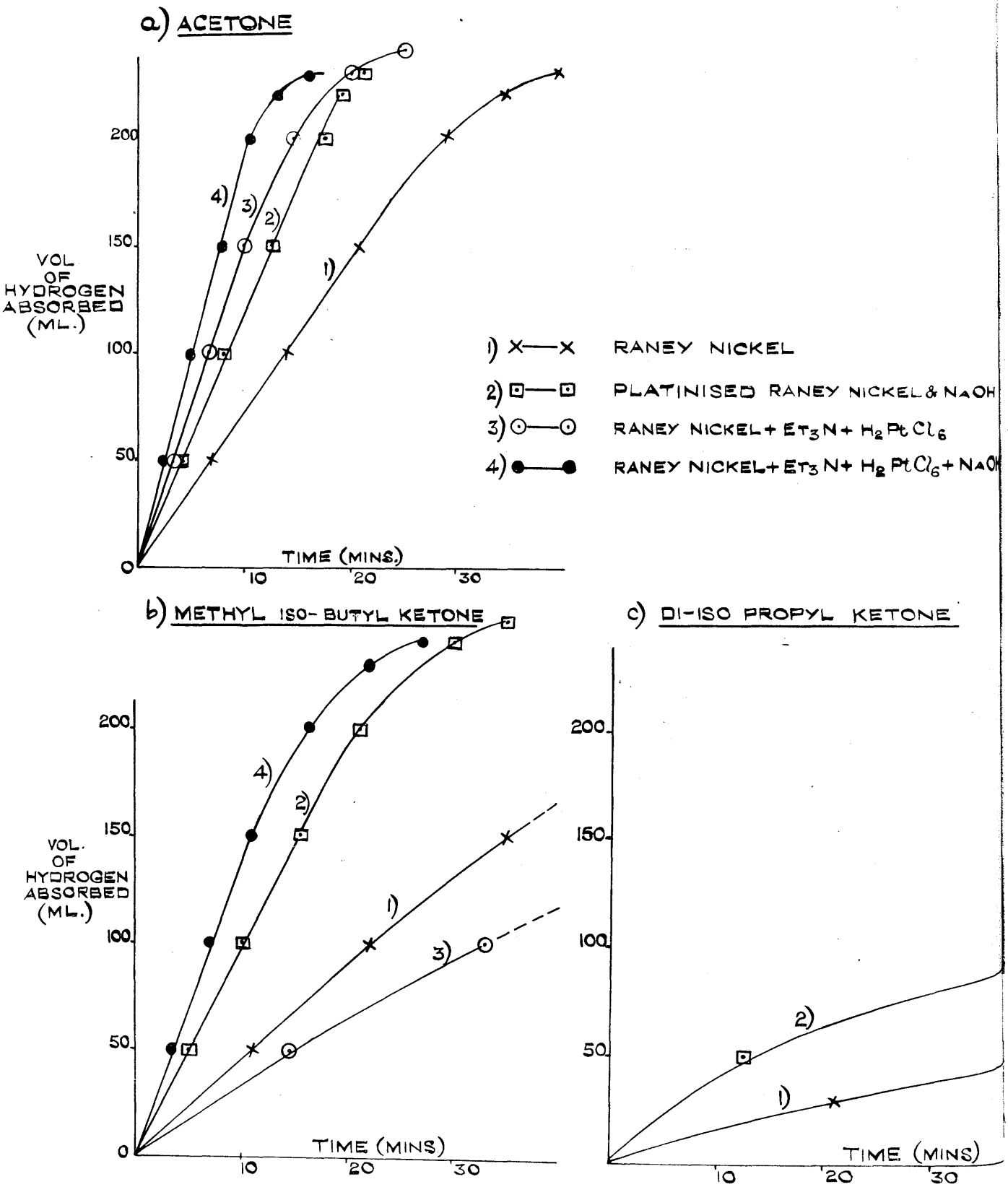


Table 1

Hydrogenation of Aliphatic Ketones at Atmospheric Pressure of Hydrogen

Substance	Time of hydrogenation (min.)						
	R.Ni	R.Ni + NaOH	R.Ni + Et_3N	Ni-Pt + NaOH	Ni-Pt + NaOH + Et_3N	R.Ni + Et_3N + H_2PtCl_6	R.Ni + Et_3N + H_2PtCl_6 + NaOH
Acetone	39	24	31	21	28	25	16
Methyl ethyl ketone	52	38	47	27	35	47	19
Methyl n-propyl ketone	76	36	64	30	38	83	21
Methyl n-amyl ketone	77	57	83	33	35	93	25
Methyl iso-butyl ketone	78	53	-	35	41	126	27
Diethyl ketone	80	-	-	37	-	221	27
Ethyl n-butyl ketone	82	-	-	38	-	265	34
Diisopropyl ketone	i.	-	-	253	-	i.	i.

For quantities of promoters see page 55.

i. - reaction incomplete.

The results show that considerable promotion of the reduction of the ketones was achieved solely by addition of sodium hydroxide to the catalyst. The effect of the addition of triethylamine was slight. Delépine's catalyst was markedly superior to untreated Raney Nickel and was not promoted by addition of triethylamine. Lieber's catalyst exhibited an anomalous behaviour in that it was superior to Raney Nickel in the hydrogenation of acetone; the superiority was less marked with methyl ethyl ketone; with higher ketones it was inferior to the untreated catalyst. When, however, sodium hydroxide was added to Lieber's catalyst pronounced promotion was obtained in every case and the most rapid hydrogenation was obtained by this means.

It was observed by Delépine (38), that his platinised catalyst without the addition of sodium hydroxide was sometimes less effective than untreated Raney Nickel. It would therefore appear that addition of sodium hydroxide to the catalyst whether platinised by Delépine's or by Lieber's method is essential in order to ensure promotion. Pattison and Degering (53), found that Raney Nickel was readily poisonned by addition of halogen compounds. Cornubert (54), effected selective hydrogenation of unsaturated carbonyl compounds by the addition of traces of halogen compound to the catalyst; inhibition of the reduction of the carbonyl group

occurred and the saturated ketone was obtained. It would therefore appear that the loss of activity of Lieber's catalyst in the hydrogenation of higher ketones is caused by chloride ion derived from chloroplatinic acid. The higher activity of Lieber's catalyst after addition of sodium hydroxide, compared with Delépine's may be attributed to more efficient dispersal of platinum on the catalyst. With the former, platinising was effected by shaking the catalyst with the yellow precipitate of $(Et_3N)_2 . H_2PtCl_6$ formed on addition of H_2PtCl_6 to Et_3N. With the latter a dilute solution of chloroplatinic acid was added to a suspension of Raney Nickel with the result that the lighter particles of catalyst were preferentially platinised.

(b) Hydrogenation at 45 p.s.i. hydrogen pressure.

The results for the hydrogenation of aliphatic ketones at 45 p.s.i. differential hydrogen pressure are given in Table 2 and Figures 2a, b and c. They are in accord with the results obtained at atmospheric pressure. Delépine's catalyst was superior to the unpromoted catalyst. Lieber's catalyst was found to be more active than Raney Nickel in the reduction of acetone, but less active in the reduction of the higher ketones. Addition of sodium hydroxide to Lieber's catalyst gave the most rapid hydrogenation in every case.

FIGURE 2.

HYDROGENATION OF ALIPHATIC KETONES AT 45 p.s.i. PRESSURE

FIG. 2.

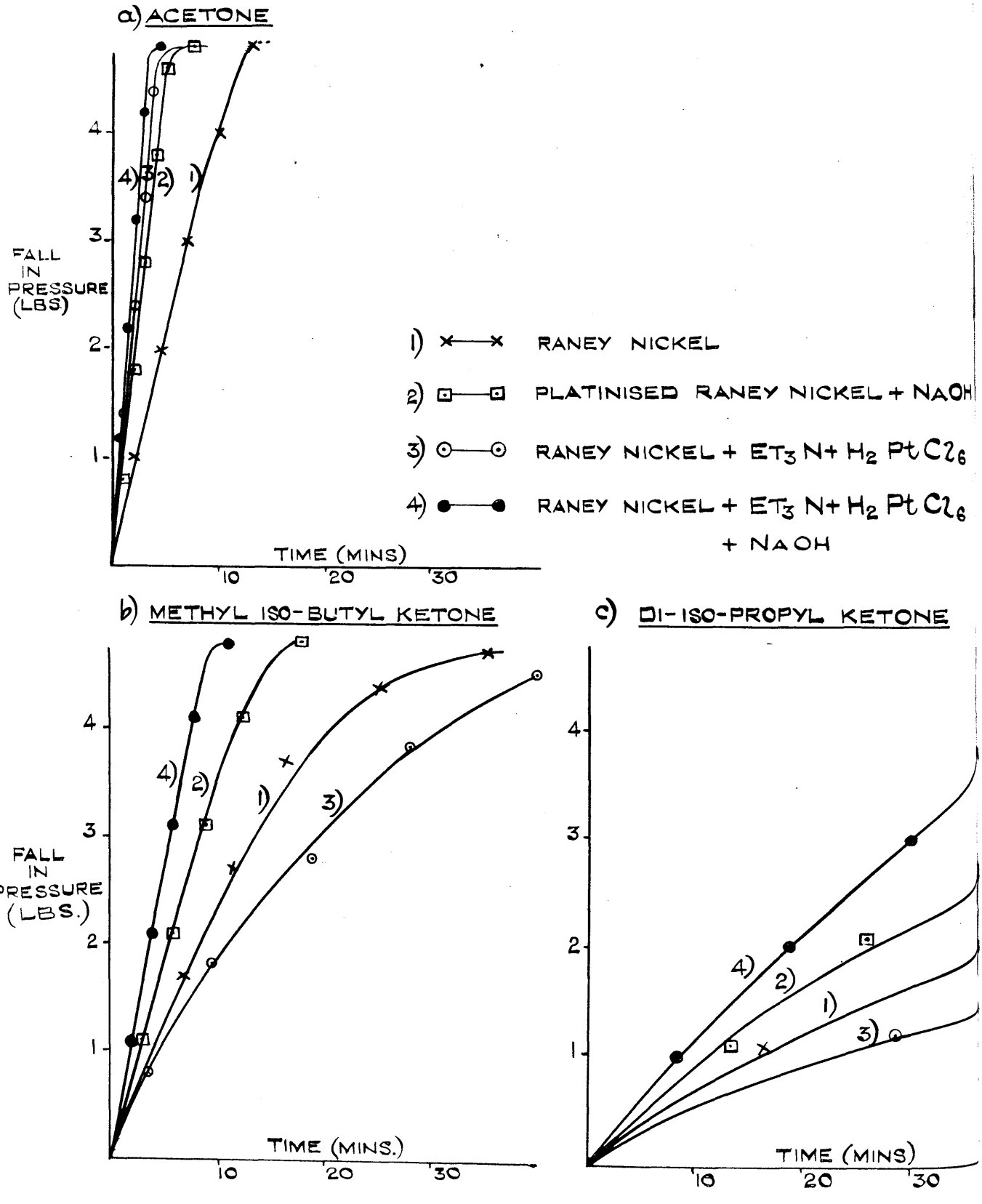


Table 2

Hydrogenation of aliphatic ketones
at 45 p.s.i. hydrogen pressure

Substance	Time of hydrogenation (min.)			
	R.Ni	Ni-Pt + NaOH	Ni + Et_3N + H_2PtCl_6	Ni + Et_3N + H_2PtCl_6 + NaOH
Acetone	13	7.5	7	4.5
Methyl ethyl ketone	19	14.5	18	6.5
Methyl n-propyl ketone	25	14	25	9
Methyl n-amyl ketone	25	15.5	46	10
Methyl iso-butyl ketone	35	18	48	11
Diethyl ketone	48	27	53	10
Ethyl n-butyl ketone	47	29	82	14
Diisopropyl ketone	277	112	i	89

For quantities of promoters see page 55.

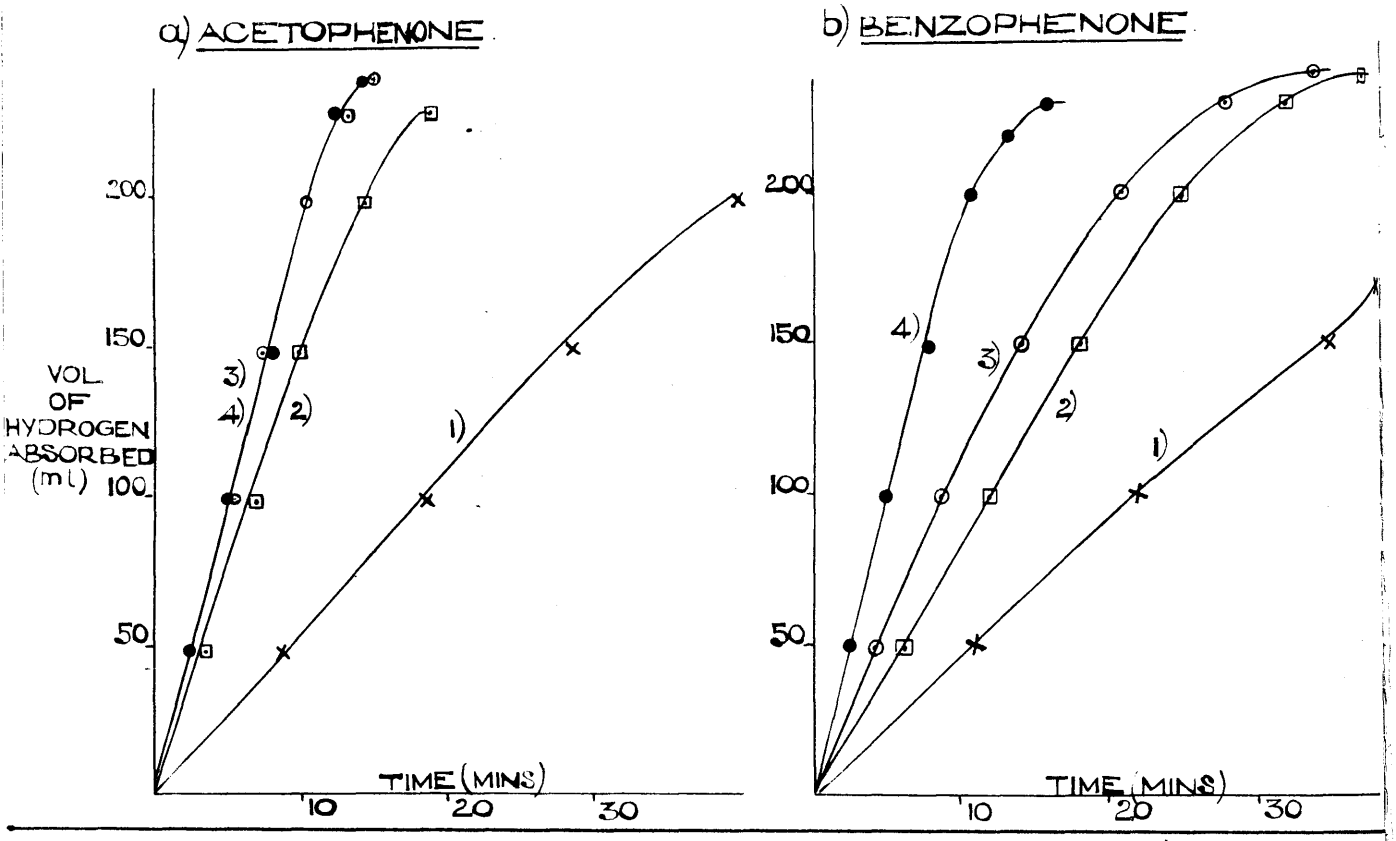
i - reaction incomplete.

Aromatic Ketones.

In the hydrogenation of aromatic ketones at atmospheric pressure (Table 3, Figures 3a, b), considerable promotion of Raney Nickel catalyst was obtained with sodium hydroxide and with triethylamine. This promotion was enhanced by using Delépine's and Lieber's catalysts. Delépine's catalyst was found to be slightly inferior to Lieber's. In marked contrast with the aliphatic ketones, addition of sodium hydroxide to

HYDROGENATION OF AROMATIC KETONES AT ATMOSPHRIC PRESSU

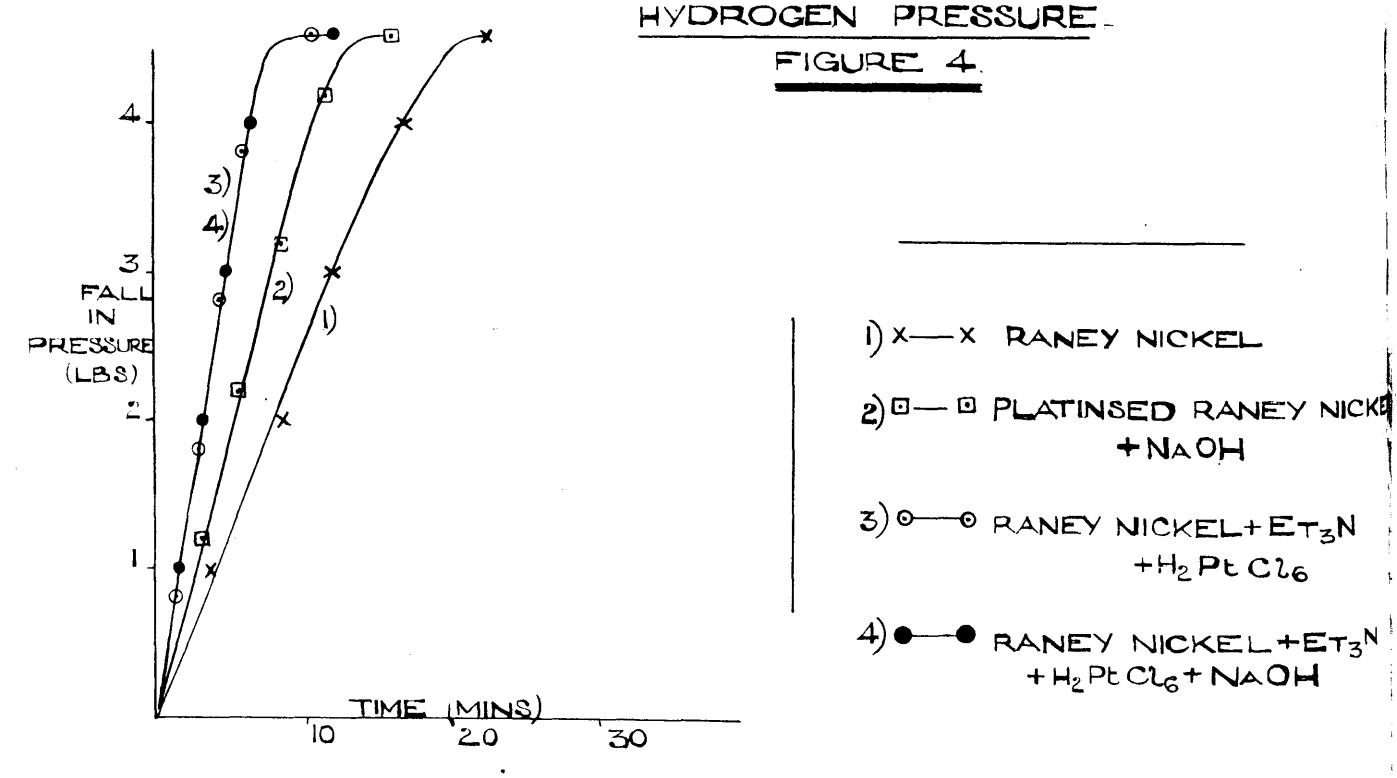
FIGURE. 3



HYDROGENATION OF ACETOPHENONE AT 45 P.S.I.

HYDROGEN PRESSURE

FIGURE 4.



the latter catalyst produced no effect in the hydrogenation of acetophenone and propiophenone, although the effect was considerable in the hydrogenation of benzophenone.

Table 3

Hydrogenation of aromatic ketones under atmospheric pressure of hydrogen

Substance	Time of Hydrogenation (mins.)						
	R.Ni	Ni + NaOH	Ni + Et_3N	Ni-Pt + NaOH	Ni-Pt + NaOH + Et_3N	Ni + Et_3N + H_2PtCl_6	Ni + Et_3N + H_2PtCl_6 + NaOH
Acetophenone	57	30	38	19	21.5	15	14.5
Propiophenone	90	55	65	34	48	24	24
Benzophenone	70	40	39	38	-	34	16

For Quantities of Promoters see page 55.

The results for acetophenone and propiophenone at 45 p.s.i. differential hydrogen pressure showed a similar trend to those at atmospheric pressure (Table 4, Fig. 4).

Table 4

Hydrogenation of aromatic ketones under 45 p.s.i. hydrogen pressure

Substance	Time of Hydrogenation (mins.)			
	R.Ni.	Ni-Pt + NaOH	Ni + Et_3N + H_2PtCl_6	Ni + Et_3N + H_2PtCl_6 + NaOH
Acetophenone	22.5	8.5	5.5	6
Propiophenone	33	16.5	10.5	12

Cyclohexanones.

The results for a series of cyclohexanones are given in Table 5 for hydrogenation at atmospheric pressure and shown graphically in Figs. 5 a-d. The results parallel those for aliphatic ketones (page 17). Once more the most pronounced promotion was obtained by addition of sodium hydroxide to Lieber's catalyst.

In the "promoted" reduction of cyclohexane-1:3-dione, the hydrogen uptake was less than theoretical; this was probably due to conversion of some of the 1:3-dione to a keto-carboxylic acid by sodium hydroxide.

The results for hydrogenation at 45 p.s.i. differential hydrogen pressure are given in Table 6 and Figures 6 a-d; they follow the trend of the results at atmospheric pressure, showing once more that Lieber's catalyst after addition of sodium hydroxide, gives the most rapid hydrogenation in every case.

FIGURE 5

HYDROGENATION OF CYCLOHEXANONES AT ATMOSPHERIC PRESSURE

FIGURE. 5

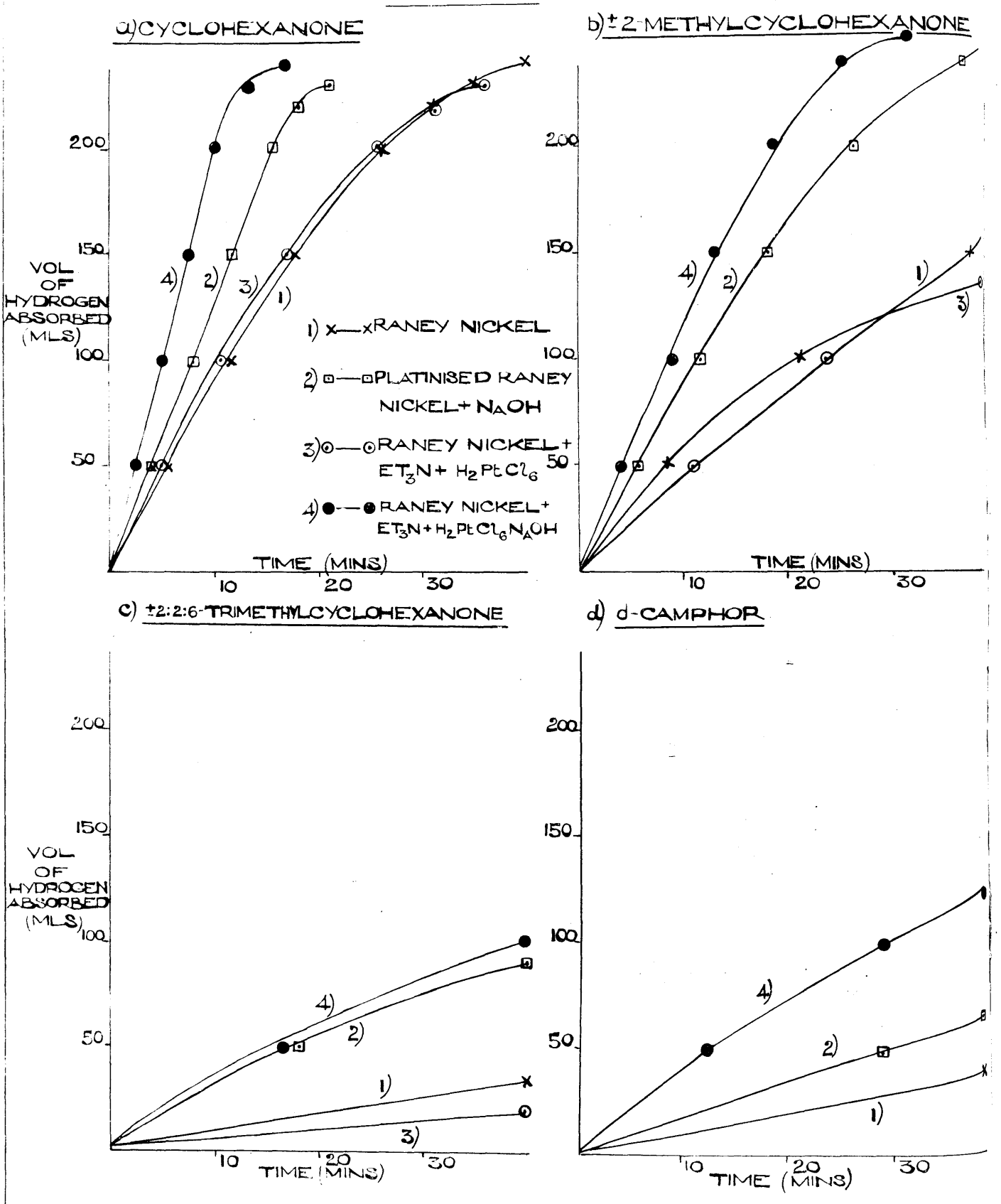


Table 5

Hydrogenation of cyclohexanones under atmospheric pressure of hydrogen

Substance	Time of Hydrogenation (mins.)					
	R.Ni	R.Ni + NaOH	Ni-Pt + NaOH	Ni-Pt + NaOH + Et_3N	Ni + Et_3N + H_2PtCl_6	Ni + Et_3N + H_2PtCl_6 + NaOH
Cyclohexanone	40	40	21	31	37	17
4-Methylcyclohexanone	60	45	23	28	36	20
± 2-Methylcyclohexanone	88	65	45	-	161	32
2:2 dimethylcyclohexanone	93	70	49	-	167	32
± 2:2:6-Tri-Me-cyclohexanone	472	-	264	-	i	200
d-camphor	580	-	329	-	-	153
2:2:6:6-Tetra-Me-Cyclo-hexanone	i	-	1600	-	-	1600
Cyclohexane-1:3-dione	250	-	-	-	-	i

For quantities of promoters see Page 55.

i - reaction incomplete.

FIGURE 6.

FIG. 6.

HYDROGENATION OF CYCLOHEXANONES AT 45p.s.i. HYDROGEN PRESSURE

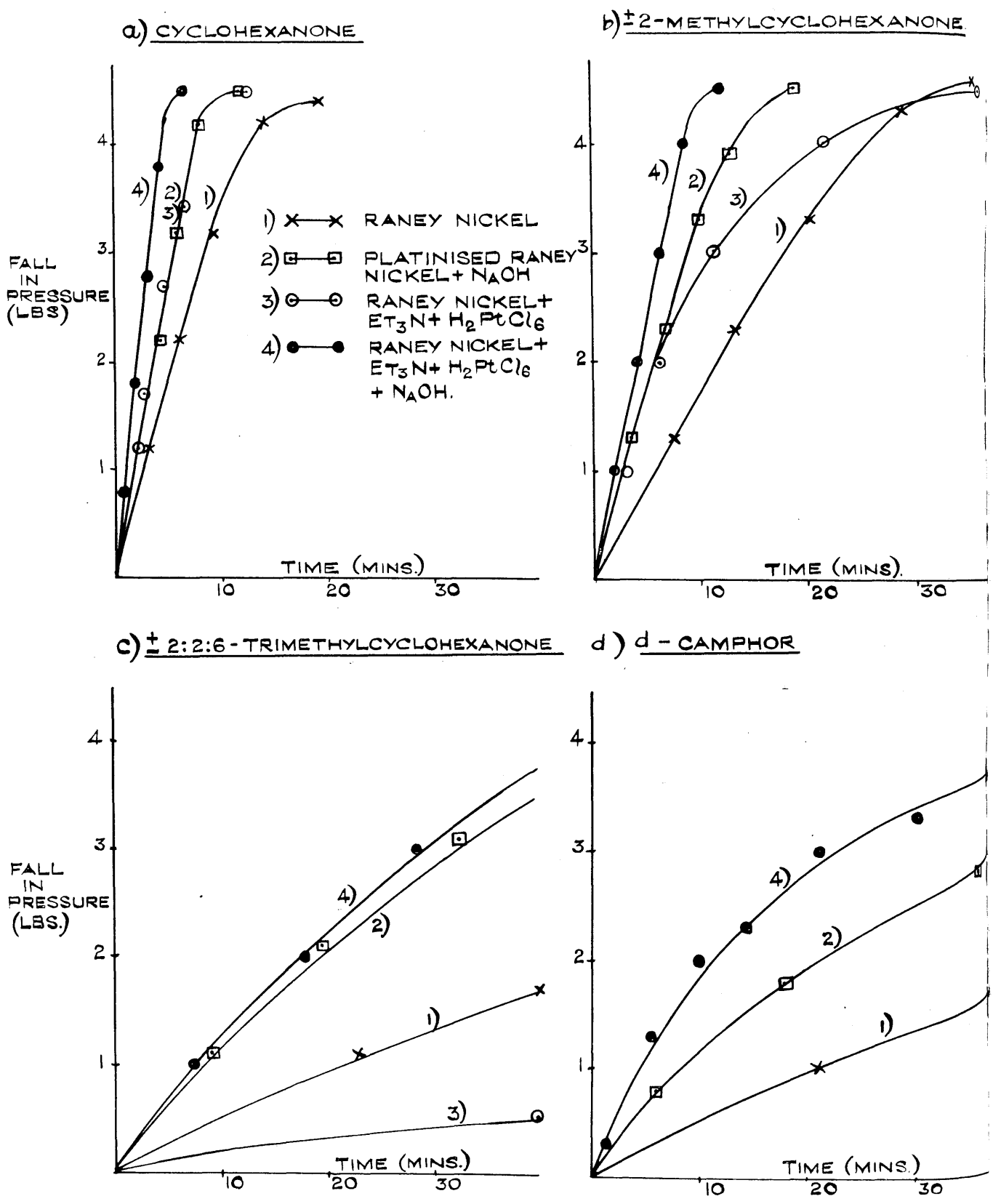


Table 6

Hydrogenation of cyclohexanones under 45 p.s.i. hydrogen pressure

Substance	Time of Hydrogenation (mins.)			
	R.Ni	Ni-Pt + NaOH	Ni + Et_3N + H_2PtCl_6	Ni + Et_3N + H_2PtCl_2 + NaOH
Cyclohexanone	19	11.5	12	6
± 3-Methylcyclohexanone	24	11.5	15	9
4-Methylcyclohexanone	24	11	15	9
± 2-Methylcyclohexanone	36	18.5	37	11.5
2:2-Dimethylcyclohexanone	36	19	42	16
± 2:2:6-Trimethylcyclohexanone	212	90	i	74
d-camphor	211	98	-	67
2:2:6:6-Tetra-Me-cyclohexanone	i	690	x	590
Fenchone	-	-	-	720

i - reaction incomplete. x - no hydrogen absorption.

For quantities of promoters see Page 55.

Cyclopentanones.

Since Delépine's promoted catalyst and the catalyst developed from Lieber's catalyst were found to be the most effective in the hydrogenation of aliphatic ketones and cyclohexanones, it was decided to use only these two catalysts in a study of the hydrogenation of a series of cyclopentanones.

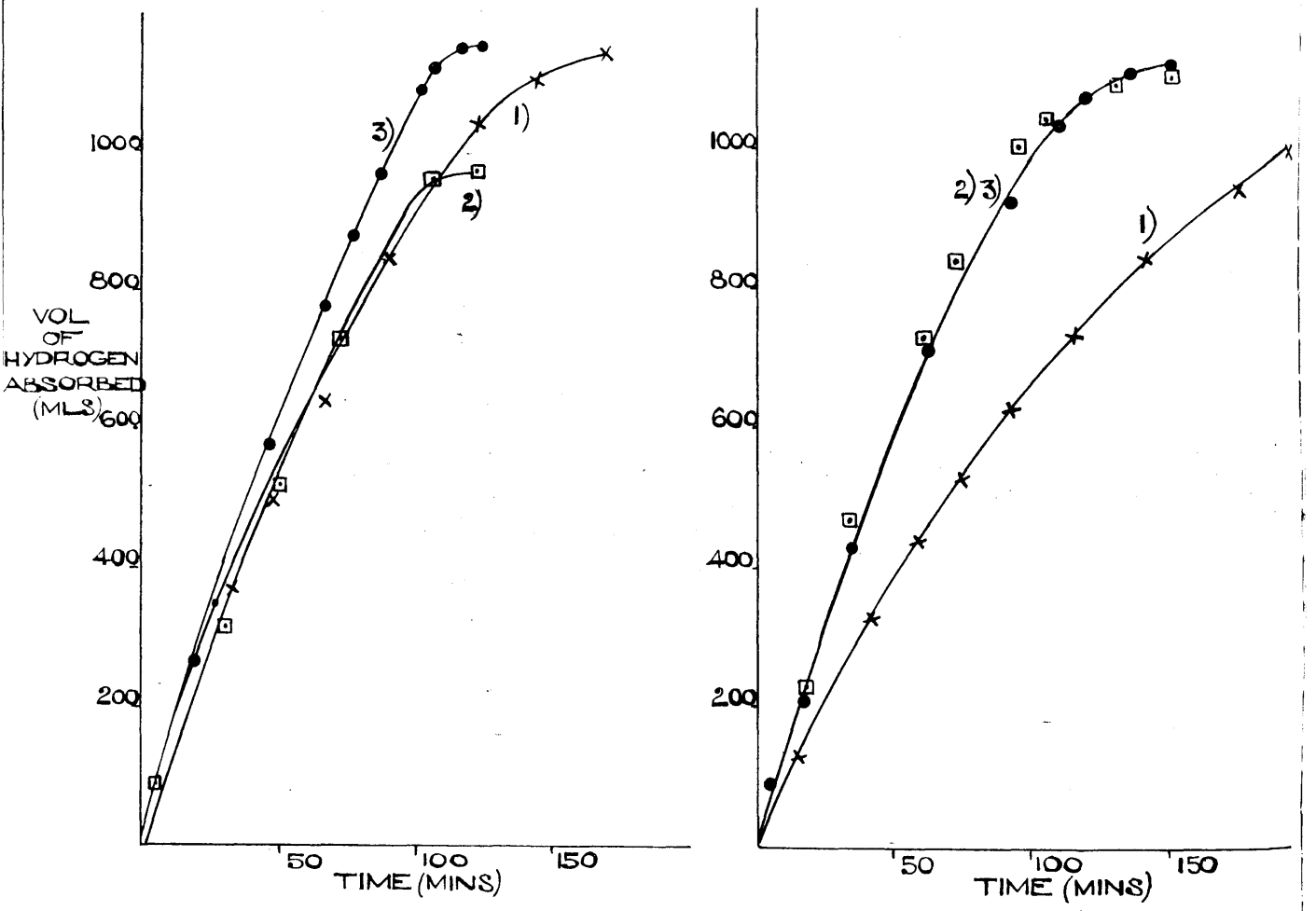
FIGURE 7.

FIGURE 7

HYDROGENATION OF CYCLOPENTANONES AT ATMOSPHERIC PRESSURE

a) CYCLOPENTANONE.

b) 2:2-DIMETHYLCYCLOPENTANONE



1) X—X RANEY NICKEL

2) ⊡—⊡ PLATINISED RANEY NICKEL + NaOH

3) ●—● RANEY NICKEL + Et_3N + H_2PtCl_6 + NaOH

In each case 0.05 g. mole of ketone in 50 ml. EtOH was hydrogenated with 2 g. catalyst. The results were compared with those for the unpromoted catalyst; they are given in Table 7 and Figures 7 a and b.

Table 7

Hydrogenation of cyclopentanones at atmospheric pressure of hydrogen

Substance	Time of hydrogenation (mins.)		
	Raney Nickel	Delépine's Catalyst	Lieber's catalyst + NaOH
Acetone	141	-	-
Cyclopentanone	170	122	123
± 2-Methylcyclopentanone	258	121	113
± 3-Methylcyclopentanone	168	118	115
2:2-Dimethylcyclopentanone	274	150	150

Considerable promotion was obtained by both methods, especially in the hydrogenation of ± 2-methyl- and 2:2-dimethyl-cyclopentanones. There was little difference in the extent of promotion by the two methods. It was observed that when cyclopentanone and ± 3-methyl-cyclopentanone were hydrogenated over Delépine's promoted catalyst, the uptake of hydrogen was less than theoretical. It would seem that some condensation of the cyclopentanone had occurred in the presence of NaOH, as was shown by the presence of a small quantity

catalyst was less active than Ni catalyst in the hydrogenation of cyclohexene and nitrobenzene; there was little difference in their activities when used for hydrogenation of acetone and cyclohexanone; the Ni-Pt catalyst was, however, more active in the hydrogenation of ± 2-methyl-cyclohexanone, ± 2:2:6-trimethylcyclohexanone, d-camphor and acetophenone.

Table 8

Comparison of the activities of Raney Nickel and Raney Nickel-Platinum Catalysts

Substance	Raney Ni.	Raney Nickel + Et_3N + H_2PtCl_6 + NaOH	Ni-Pt	Ni-Pt + NaOH
Cyclohexene	14	-	27	-
Nitrobenzene	29	-	38	-
Acetone	39	16	41	23
Cyclohexanone	40	16	40	27
± 2-Me-cyclohexanone	88	31	54	28
± 2:2:6-Tri-Me-cyclohexanone	472	201	352	159
d-camphor	580	153	273	155
Acetophenone	57	15	37	23

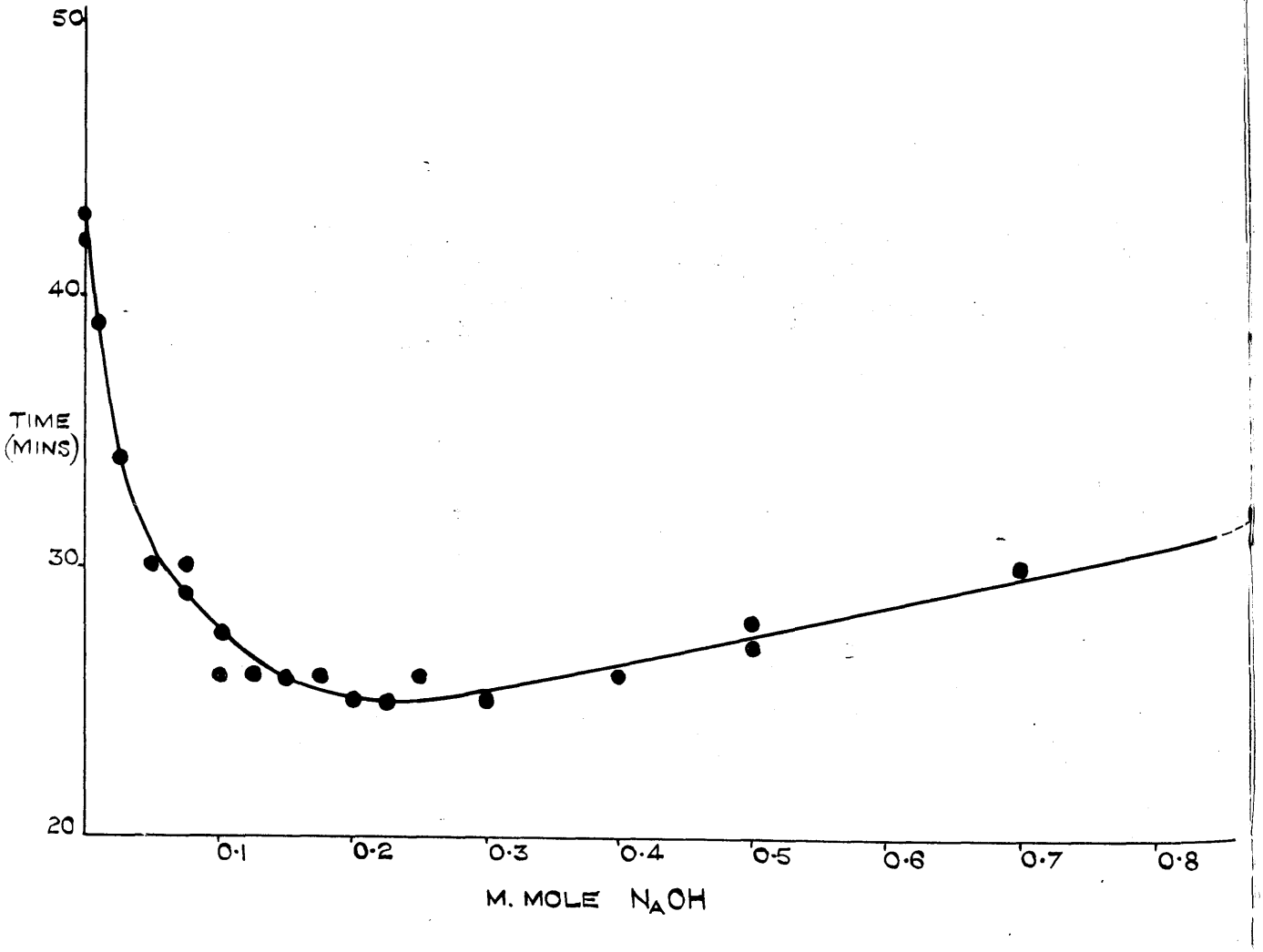
The figures given are the times (mins.) for hydrogenation of 0.01 g. mole of substance w. 0.5 g. catalyst.

When the Ni-Pt catalyst was compared with Lieber's Raney Nickel promoted with sodium hydroxide in the hydrogenation

FIGURE 8.

FIG. 8.

— PROMOTION OF HYDROGENATION OF ACETONE —
(EFFECT OF THE AMOUNT OF N_AOH ON THE TIME OF HYDROGENATION OF 0·01 MOLE OF ACETONE OVER 0·5g. RANEY NICKEL CATALYST.)



of these ketones, it was found to be less active (Table 8). Upon addition of sodium hydroxide to it, their activities were found to be of similar magnitude although the amount of platinum present in the Ni-Pt catalyst was approximately double that in the Lieber catalyst. This difference might be attributed to the fact that a considerable amount of the platinum was buried within the particles of the alloy catalyst and so was ineffective.

A study of the effect of ageing of the catalyst in the hydrogenation of acetone (experimental p.59), showed that the Ni-Pt alloy catalyst retained much of its initial activity for a longer time than the nickel catalyst.

Promotion of Raney Nickel catalyst with alkali.

An investigation of the effect of concentration of sodium hydroxide in the promotion of the hydrogenation of acetone over Raney Nickel (experimental p.63), showed that the promotion given by 0.1 ml. of hydroxide solution increased to a maximum when the normality was in the range IN to 3N, and then decreased with further increase in the strength of the hydroxide solution. The results are illustrated in Figure 8. The decrease in activity of the catalyst when excess sodium hydroxide was added, may be due to geometric blockage of the surface as predicted by Dowden (5).

No critical concentration of promoter was observed.*

Sodium hydroxide was found to be strongly adsorbed on the catalyst surface (experimental p. 59). It was thought that if promotion were due to adsorbed sodium ion, lithium hydroxide might function better as a promoter since the ionic radii of lithium and nickel are of similar magnitude. Results indicated that it was slightly superior since hydrogenation times for a series of ketones over Raney Nickel promoted with lithium hydroxide were 20% less than the times obtained with the sodium hydroxide promoted catalyst (experimental p. 60). Potassium hydroxide was a less efficient promoter than sodium hydroxide since the times for reduction of methyl ethyl ketone over Raney Nickel promoted with these two substances were in the ratio 1.17:1, and of methyl n-butyl ketone 1.33:1.

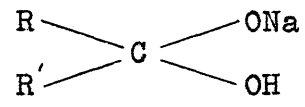
After the addition of sodium hydroxide to hydrogen saturated Raney Nickel catalyst a further adsorption of hydrogen was observed (p. 61). This result indicates that alkali also promotes the adsorption of hydrogen, and that the active surface of the catalyst is increased by addition of alkali (see p. 10, Smith et al.).

Various mechanisms for the promotion of Raney Nickel by sodium hydroxide have been advanced. Delépine pointed out

---

*Griffith (55), in an investigation of the promotion of molybdenum oxide catalyst in the decomposition of cyclohexane and hexane, found that an extremely critical concentration of promoter gave optimum promotion effect.

that alkali could not promote reduction via the enol form of the ketone since the hydrogenation of ketones such as benzophenone with no α-hydrogen atom was promoted by alkali. An improbable mechanism was put forward by Delépine (40), who explained the role of sodium hydroxide in the hydrogenation of carbonyl compounds by the formation of an addition compound with the ketone:-



He suggested that the addition compound would then be readily hydrogenolysed because of the mobility of the ONa group. Dupont and Piganiol (56), proposed that addition of metallic oxides to Raney Nickel catalyst led to the formation of areas of non-metallic phase on the crystallite surface. The promoter would strongly adsorb the hydrogen acceptor while the metal catalyst adsorbed hydrogen so that points of contact between the metal catalyst and the promoter would become the active sites of the catalyst at which interaction between hydrogen and unsaturated compound occurred. Such a mechanism does not account for further adsorption of hydrogen on addition of alkali to the catalyst.

If the promotion were due solely to an increase in the amount of hydrogen adsorbed on the catalyst, the promotion

effect of alkali would not be confined to the hydrogenation of carbonyl compounds. A study of the hydrogenation of cyclohexene did not confirm this. It was found that sodium hydroxide retarded the hydrogenation of cyclohexene (experimental p.61), and although it caused a sharper completion of reaction, it had no effect on the initial rate of hydrogenation of nitrobenzene (experimental p.62). Moreover Cornubert and Phélisse (57), in a study of the selective hydrogenation of unsaturated ketones, confirmed that alkali is a promoter only of the ketone ⟶ alcohol reaction.

Schmidt (58), has related the rate of liquid phase hydrogenation of ethylenes to the value of the heat of adsorption of the solvent which is a function of its heat of vaporisation. He found that the hydrogenation was retarded in solvents of high heat of vaporisation. In the present work, it was found that the activity of the catalyst was enhanced by the presence of sodium hydroxide in cases where the heat of vaporisation of the product of hydrogenation was substantially greater than that of the reactant, (Table 11). In such cases it would therefore appear that sodium hydroxide is overcoming a retardation of reaction due to the products of hydrogenation.

Table 11

Heats of vaporisation of hydrogen acceptors and their products of hydrogenation

Substance	Heat of vaporisation* k. cals.	Hydrogenation product	Heat of vaporisation k. cals.	Effect of NaOH
Cyclohexene	7.28	Cyclohexane	7.34	Retardation
Acetone	7.26	2-Propanol	9.56	Promotion
Methyl ethyl ketone	7.59	2-Butanol	9.92	"
Cyclohexanone	9.50	Cyclohexanol	10.70	"
Nitrobenzene	7.94	Aniline	9.71	Slight promotion

* Values obtained from Landolt-Bornstein.

Bremner and Keeys (59), regarding the catalyst as a Lewis acid or base, suggested tentatively that addition of alkali to Raney Nickel catalyst in the hydrogenation of ketones, modifies the work function of the catalyst, thus increasing the electron donor characteristic. More rapid desorption of the alcohol product occurs therefore and the surface of the catalyst available for adsorption of fresh ketone is increased and with it the rate of hydrogenation. This mechanism accounts most satisfactorily for the experimental observations of the present work. It may also be

assumed that in these hydrogenations the solvent ethanol is adsorbed to some extent. The promotion of adsorption of hydrogen may therefore be interpreted in a similar way, viz., that modification of the electron donor characteristic of the catalyst by addition of alkali causes desorption of some ethanol and hydrogen is adsorbed on the freed surface. It would therefore seem that the function of alkali in the promotion of the hydrogenation of ketones is to modify the properties of the surface of Raney Nickel in such a way that the product of hydrogenation is readily desorbed and the concentration of reactants at the surface is increased.

EXPERIMENTAL

Preparation of materials.

(a) Raney Nickel Catalyst. W-4 Raney Nickel Catalyst was used throughout this work. It was prepared by the method of Adkins and Pavlic (26), with one modification - the continuous washing process was carried out in one hour, the whole preparation taking from 3½ to 4 hours. The catalyst was prepared from 100 gm. batches of Ni-Al alloy (50:50 by weight, 80 to dust, and was stored in a 250 ml B.34 quickfit flask, carefully stoppered to exclude air.

(b) Purification of solvents and hydrogen acceptors.

Methyl and ethyl alcohols were shaken with Raney Nickel catalyst (1 g. per 100 ml) and distilled.

Dioxan (150 ml) was refluxed over sodium (9 g.) for six hours and distilled. b.102.5-103.0.

Water. Distilled water was used in the preparation of Raney Nickel, and as a solvent for hydrogenation of acetone.

Hydrogen acceptors. 100 g. of hydrogen acceptor was shaken with 10 g. Raney Nickel for ten minutes in order to remove catalyst poisons. The nickel was filtered off and the hydrogen acceptor dried over magnesium sulphate (20 g.). The hydrogen acceptor was then distilled through a six-inch bead-packed column and the appropriate fraction collected.

Modifications in the Raney Nickel treatment were made in the case of camphor and benzophenone. With these two substances, a solution in ethyl alcohol was shaken up with the catalyst, and the ketone was recovered from the alcohol. The fenchone was of technical grade; it was fractionally distilled through a 16 inch column. The fraction b 203-5 was freed from camphor with semicarbazide hydrochloride (60), steam distilled, dried over magnesium sulphate, and fractionally distilled once more.

Because of a disproportionation reaction, (61), cyclohexene could not be treated with Raney Nickel. Instead it was twice distilled through a six-inch bead packed column, after having been dried over magnesium sulphate.

Acetone	b_{755}	56.5-57	ANALA R grade.
Methyl ethyl ketone	b_{765}	79.5-80	
Methyl n-propyl ketone	b_{755}	100.5-101.5	Supplied by Light & Co.
Methyl n-amyl ketone	b_{740}	149-150	
Methyl iso butyl ketone	b_{757}	116.5-117.5	
Diethyl ketone	b_{755}	101-102.5	
Ethyl n-butyl ketone	b_{765}	155-156	
Diisopropyl ketone	b_{765}	139-140	
± 3-Methylcyclohexanone	b.	168.5-169.5	
± 4-Methylcyclohexanone	b_{740}	169-170	
Cyclohexanone	b_{747}	154-155	

± 2-Methylcyclohexanone	b. 165-166	Supplied by Glaxo Laboratories, Ltd.
2:2-dimethylcyclohexanone	b_{757} 171.5-172	
± 2:2:6-trimethylcyclohexanone	b. 182-183	
2:2:6:6-tetramethylcyclohexanone	b_{762} 185-186	
d-camphor	$[\alpha]_D^{20}$ 44.1	Supplied by Whiffen & Co.
Fenchone	$n_{17.5}$ = 1.4632 b. 203	Supplied by B.D.H.
Acetophenone	b. 200	Supplied by B.D.H.
Propiophenone	b. 115-115.5	" " Light & Co.
Benzophenone	m. 49	" " B.D.H.
Cyclohexene	b. 84-84.5	" " Light & Co.
Nitrobenzene	b. 208-209	" " Hopkins & Williams.

Preparation of Cyclopentanone (62).

Adipic acid (200 g.) was mixed intimately with finely powdered barium hydroxide (10 g.). The mixture was heated in a 1 l. distilling flask in an air bath to 285 to 295° C. (thermometer in the mixture) for 4 hours, and the cyclopentanone which slowly distilled, was collected, separated from water in the distillate, dried with potassium carbonate and distilled (yield 89 g., b.128-131°). The cyclopentanone was then fractionally distilled through a bead-packed column. The fraction, b. 130.0-130.6, (71 g.) was retained.

Preparation of 3-Methylcyclopentanone (63).

850 cc. HNO_3 (d.1.42) were heated in a 2 l. pyrex flask equipped with dropping funnel and 10 in. Davies double surface condenser. When the acid was boiling vigorously, 4-Methylcyclohexanol (250 g.) was added slowly (3 hours), the flask was heated for a further 20 minutes, and the reaction mixture was then diluted with water (850 ml.), and saturated with ammonium sulphate. The mixture was extracted with ether (3 x 500 ml.) and dried over anhydrous sodium sulphate. The ether was distilled off, and the residue was distilled under reduced pressure until the pressure rose rapidly to 100 mm. and the temperature rose to 160° C. The residue was then heated slowly, with a thermometer in the residue, to 300-320° C. The bulk of the distillate came over at 310-314° C. It was washed with potassium carbonate solution (10%), dried over potassium carbonate, and distilled - b. 141-3, yield 88 g. 40%. The 3-methylcyclopentanone was then fractionally distilled through a bead packed column, the fraction boiling 142.8-143.3 (75 g.) being retained.

Preparation of 2-methylcyclopentanone (64).

Adipic acid (200 g.), ethyl alcohol (150 g.) and benzene (360 g.) were refluxed for five hours with sulphuric acid (60 g.). After cooling, the benzene layer was separated and neutralised by shaking it with 10% sodium carbonate; the

benzene was distilled off, and the residue distilled under reduced pressure. Diethyl adipate (220 g., 80% yield, b_{18} 130-132) was thus obtained.

Sodium (24 g.) was powdered in dry thiophen-free toluene (400 ml.) in a 2 l. flask equipped with a high speed stirrer, double surface condenser and dropping funnel. With constant stirring, diethyl adipate (200 g.) was added at a sufficient rate to keep the toluene refluxing (1 hr.); the flask was refluxed for one hour after the addition, then cooled to -15° C. Methyl iodide (55 ml.) was added slowly with stirring ($\frac{1}{2}$ hr.), stirring was continued for $\frac{1}{2}$ hr., and excess methyl iodide was distilled off. Water (100 ml.) was added to the reaction mixture, and separated from the toluene layer; the aqueous solution was then extracted with more toluene (2 x 75 ml.): the toluene extracts were combined, cooled to 0° C., extracted with 10% potassium hydroxide, washed with dilute sulphuric acid (10% solution), then sodium carbonate (10% solution). The toluene was distilled off, and the residue of 2-Methyl-2-ethylcarboxycyclopentanone was distilled under reduced pressure (b_{20} 138-140, yield 133 g.)

Hydrolysis of 2-methyl-2-ethylcarboxycyclopentanone was accomplished by refluxing with dilute hydrochloric acid (400 ml. conc. HCl + 200 ml. H_2O) for 24 hours. The mixture was extracted with ether, the ether was removed by distillation,

and the residue of 2-methylcyclopentanone was distilled. Further purification was obtained by distillation through a bead-packed column, the fraction b. 138.5-139, (65 g.) being retained.

Preparation of 2:2-dimethylcyclopentanone (65).

2-methylcyclopentanone (114 g.) was added slowly (2 hours) with stirring to finely ground sodamide (45.5 g.) under dry ether (1 l.) contained in a dry 2 l. flask. The reaction mixture was refluxed for 3 hours; cooled; methyl iodide (75 ml.) was added slowly (2 hours); the reaction mixture was refluxed for 2 hours, and cooled; water (200 ml.) was added; the ether layer was separated; the aqueous layer was extracted with ether which was combined with the main ether fraction, washed with dilute sulphuric acid, and then dilute sodium carbonate (10% soln.). The ether extract was dried over potassium carbonate; the ether was distilled off and the residue fractionated. The main fraction (b. 142.5-144.5, 57 g.) was purified via the semicarbazone (m. 190-191) and redistilled, b. 143.3-143.5.

Hydrogenation Apparatus.

(a) A conventional apparatus for hydrogenation at atmospheric pressure was used (Figure 9). It consisted of a flask of 200 ml. capacity, connected to a gas burette and

FIGURES 9 & 10.

FIGURE 9. APPARATUS FOR HYDROGENATION AT ATMOSPHERIC PRESSURE.

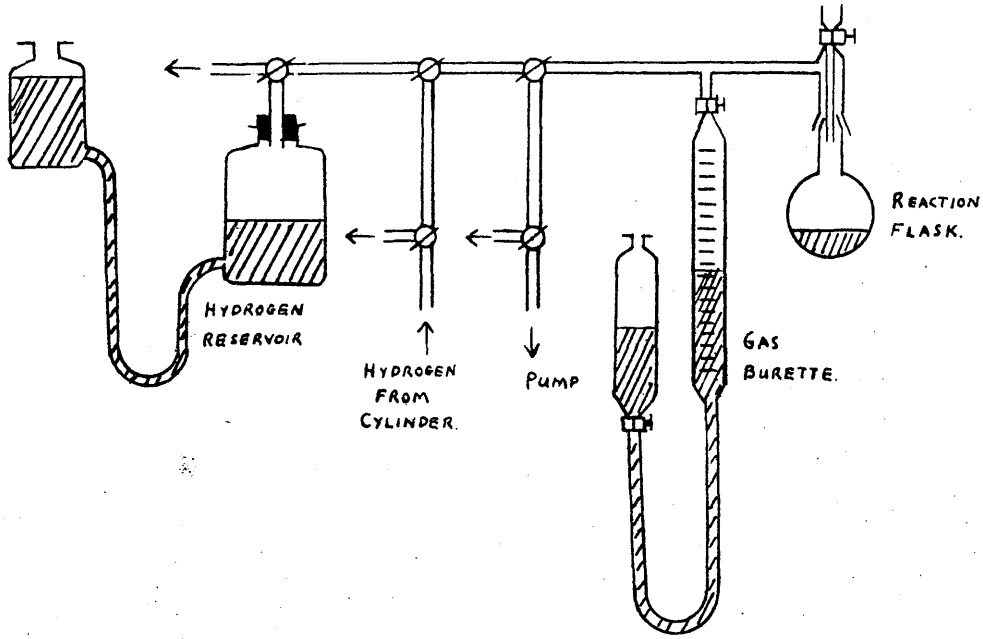
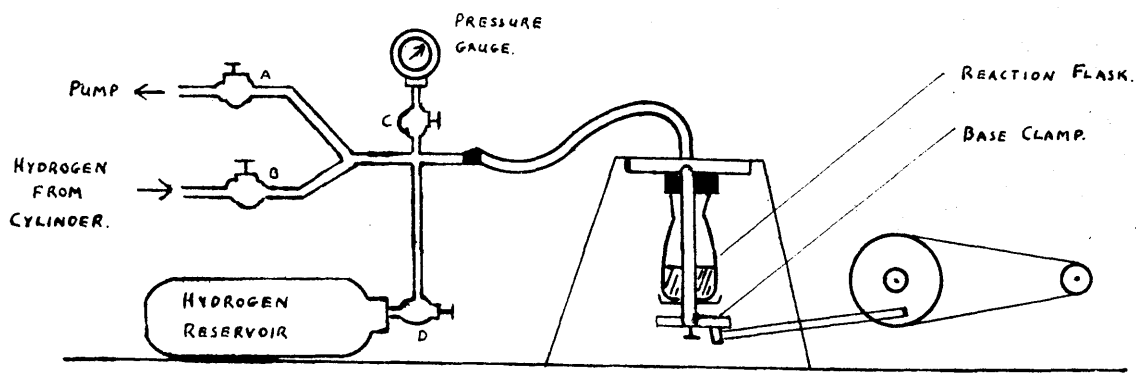


FIGURE 10. APPARATUS FOR HYDROGENATION AT 45 p.s.i. DIFFERENTIAL PRESSURE.



hydrogen reservoir with entry and exit for evacuating the apparatus and filling it with hydrogen. The reaction flask was fitted with a small funnel and stopcock through which promoters etc. could be added. The flask was shaken at a speed of 200 double strokes per minute. All connections in the apparatus were of plastic tubing to prevent possible contamination with sulphur.

The procedure for each hydrogenation was as follows:- the catalyst solvent and hydrogen acceptor were added to the reaction flask which was then connected up to the rest of the apparatus. Air was displaced by evacuating the apparatus three times and refilling it with hydrogen. As soon as the flask was shaken the take up of hydrogen commenced and was followed throughout the reaction by noting the time for absorption of successive 10 ml. volumes of hydrogen. Cylinder hydrogen was used without further purification since Skelly (44), had found that purification by diffusion through a palladium thimble had a negligible effect on the rate of hydrogenation. Cranstoun confirmed this by showing that commercial hydrogen bubbled through Raney Nickel catalyst (to remove poisons), was not appreciably more efficient than untreated hydrogen,(75).

(b) An apparatus for hydrogenation at 45 p.s.i. differential pressure was assembled. It is illustrated in Figure

10 (opposite p. 41). It consisted of a reaction flask of 150 ml. capacity, connected by means of reinforced rubber tubing to a hydrogen reservoir which was fitted with valves to allow evacuation of the apparatus and filling with hydrogen. The reaction flask was clamped into position: it was shaken at a rate of 250 double strokes per minute. The procedure adopted in using the apparatus was as follows:- the reaction flask with contents made up to a volume of 40 ml. was clamped into position; the apparatus was evacuated twice and filled with hydrogen by appropriate manipulation of valves A and B; valves C and D were opened and hydrogen was admitted from the cylinder through B until the pressure reached 45 p.s.i.; valve B was then closed. The flask was shaken and the course of hydrogenation was followed by the fall in pressure registered by the Bourdon gauge.

Measurement of Raney Nickel Catalyst.

The catalyst was measured by carefully spooning it out under alcohol into a measure which had been calibrated by weighing the amount of catalyst filling it to known graduations. The measure was calibrated for each preparation of Raney Nickel.

Platinisation of Raney Nickel (Delépine and Horeau (38)).

The catalyst (3.0 g.) was suspended in a 50 ml. measuring

cylinder to about $\frac{3}{4}$ of the height of the cylinder by means of rapid stirring. Aqueous chloroplatinic acid solution (6 ml. = 0.22 m. moles) was added slowly over a period of ten minutes, followed by sodium hydroxide solution (0.2 ml. 10 N). The catalyst was then washed three times with distilled water and three times with ethanol. It was transferred under ethanol to the hydrogenation flask.

Preliminary Experiments on the hydrogenation of acetone and methyl ethyl ketone.

(a) Effect of solvent.

0.01 g. mole. of acetone in 20 ml. of solvent was hydrogenated over Raney Nickel catalyst (0.5 g.) and also over the catalyst (0.5 g.) promoted with sodium hydroxide (1.0 m. mole.). Table 12 summarises the experimental results.

Table 12

Effect of solvent on the hydrogenation of acetone.

Solvent	Time (mins.) for hydrogenation	
	Raney Nickel	Raney Nickel + NaOH
Methanol	43	31
Ethanol	45	36
Water	93	90
Dioxan	148	186

(b) Effect of added air on the rate of hydrogenation.

Willstätter (66), found that smooth hydrogenation of substances such as phthalic and maleic acids in the liquid phase with platinum catalyst was dependent on the continued presence of small amounts of oxygen in the system. The effect of oxygen (added as air) on platinised Raney Nickel was therefore investigated. Methyl ethyl ketone (1.0 g.) in ethanol (20 ml.) was hydrogenated over platinised Raney Nickel (0.5 g.) to which varying amounts of air had been admitted. The experimental results (Table 13) indicated that air caused pronounced retardation.

Table 13

Effect of addition of air to platinised Raney Nickel

Vol. of air added (ml.)	Time for hydrogenation of 1g. Me CO Et (mins.)
-	34
0.5	34
1.2	60
2.5	80
5.0	121

Carothers and Adams (67), found that small amounts of iron salts prolong the active life of a platinum catalyst without the necessity of reactivation with oxygen. When

ferrous chloride (5.0 mg.) was added to platinised Raney Nickel (0.5 g.) the rate of hydrogenation of methyl ethyl ketone fell from 10 ml. hydrogen absorption in 76 secs. to 10 ml. in 100 secs., indicating that retardation occurred.

(c) Effect of variation in the amount of catalyst.

In Table 14, the results are recorded for hydrogenation of methyl ethyl ketone (0.01 mole.) in 20 ml. ethanol with various amounts of catalyst at atmospheric pressure.

Table 14

Variation in the rate of hydrogenation at atmospheric pressure with the amount of catalyst

Wt. of Catalyst	Initial rate of hydrogenation. ml/min.	$k_{1.0}$	Time of Hydrogenation (mins.)	$t_{1.0}$
0.51	5.5	10.8	55	28
1.00	11.5	11.5	29	29
1.33	14.3	10.8	21	28
1.50	16.7	11.1	18	27
1.81	20.0	11.0	16	29
2.23	25.0	11.2	13	29

$k_{1.0}$ is the rate expressed as ml. of hydrogen absorbed per minute, and $t_{1.0}$ is the total time of hydrogenation adjusted for one gram of catalyst, assuming that the rate varied

directly with the amount of catalyst. The results show that this was so.

The results for hydrogenation at 45 p.s.i. differential pressure are given in table 15. Methyl ethyl ketone (0.05 mole.) in ethanol (40 ml.) was hydrogenated over the various quantities of catalyst detailed. The rate of hydrogenation was calculated using the following expression:-

$$k_{1.0} = \frac{2.303}{\pi t} \log \frac{P^{\circ}_{H_2}}{P_{H_2}}$$ (Smith and Fuzek (68)).

where $k_{1.0}$ = velocity constant for 1 g. of catalyst.

π = mass of catalyst used.

$P^{\circ}_{H_2}$ = initial hydrogen pressure = initial gauge reading + atmosphere pressure.

P_{H_2} = hydrogen pressure after time interval t.

The rate equation assumes that the reaction rate is first order with respect to hydrogen pressure, zero order with respect to concentration of hydrogen acceptor, and directly proportional to the mass of the catalyst.

Table 15

Variation in the rate of hydrogenation at 45 p.s.i. differential pressure with the amount of catalyst

Wt. of catalyst	$k \times 10^{-3}$	$k_{1.0} \times 10^{-3}$	Time of Hydrogenation (mins.)	$t_{1.0}$ (mins.)
0.63	0.63	1.01	238	150
1.03	1.69	1.64	79	81
1.52	2.55	1.68	38	58
1.98	3.13	1.58	29	57
2.81	4.84	1.72	21	59
3.15	5.33	1.68	19	60

With the smaller amounts of catalyst (0.5-1.0 g.) some deviation from direct proportionality was observed.

(d) Effect of variation of the initial hydrogen pressure.

Acetone (0.05 mole) was hydrogenated in ethanol (40 ml.) over Raney Nickel catalyst (3.0 g.) with initial differential hydrogen pressures of 20 and 45 p.s.i. The results (table 16) showed that the time of hydrogenation was decreased by increase in the initial pressure; the rate of hydrogenation was independent of the initial hydrogen pressure.

Table 16

Effect of initial hydrogen pressure on rate of hydrogenation

Initial pressure (p.s.i.)	t (mins.)	$k_{1.0}$
20	24	2.27
45	15	2.25

(e) Effect of copper and lead in Raney Nickel alloy.

Dowden and Reynolds (8), showed that the catalytic activity of nickel declined by alloying it with copper. The amounts of copper and lead in the nickel-aluminium alloy used for the preparation of Raney Nickel catalyst in the present work were therefore estimated - copper 0.02%, lead 0.01%. It was decided that the presence of such small quantities of these two elements would be unlikely to cause an appreciable effect upon the activity of the catalyst.

(f) Ageing of Raney Nickel catalyst.

A batch of Raney Nickel catalyst was prepared and stored under ethanol in a 250 ml. QQ flask. The flask was carefully stoppered to ensure that no air bubble remained. At various times after the preparation, 0.01 g. mole. of acetone was hydrogenated with approximately 0.5 g. of catalyst in 20 ml.

ethanol, and the time of hydrogenation was noted. A further 0.01 g. mole acetone was added with a 1.2 m. mole NaOH, and the time for hydrogenation was again found. The results are given in table 17; the rate and time of hydrogenation were adjusted for 1 g. of catalyst.

Table 17

Effect of ageing on the activity of Raney Nickel catalyst

No. of days after preparation of catalyst.	Raney Nickel		Raney Nickel + NaOH	
	Rate of hydrogenation $k_{1.0}$ ml.H_2/min.	Time for hydrogenation $t_{1.0}$ (mins.)	Rate of hydrogenation $k_{1.0}$ ml.H_2/min.	Time for hydrogenation $t_{1.0}$ (mins.)
2	16.5	19	17.6	15
3.5	14.4	20	17.8	17
10	12.7	24	15.8	19
34	9.0	33	14.8	21
74	7.4	40	12.6	23

There was a considerable decrease in activity of the catalyst with time in agreement with the results of Pattison and Degering (37). Addition of sodium hydroxide to the catalyst was found to overcome the ageing effect to a considerable extent since the loss in activity of the promoted catalyst with time was appreciably smaller.

(g) Initial promotion experiments.

The effect of small doses of amine on the rate of hydrogenation of 1.0 g. methyl ethyl ketone in 20 ml. ethanol over Raney Nickel and platinised Raney Nickel was investigated. 1.0 g. catalyst was used in each run. Towards the end of each experiment 1.2 m. mole. sodium hydroxide (solution) was added to the hydrogenation system and any effect on the reaction rate was again noted.

Table 18

Effect of organic bases on Raney Nickel and Platinised Raney Nickel

Substance	Amount of substance added m.moles	Rate of hydrogenation, secs. for 10 ml. absorption					
		Raney Nickel			Platinised Raney Nickel		
		Before addition of amine	After addition of amine	After addition of NaOH	Before addition of amine	After addition of amine	After addition of NaOH
Triethylamine	0.08	70	60	-	90	60	-
Trimethylamine	0.08	70	73	80	85	75	35
Triethanolamine	0.08	70	95	80	80	110	45
Morpholine	0.11	70	95	85	83	100	60
Tribenzylamine	0.06	80	85	80	87	97	55
Triphenylamine	0.03	100	115	70	90	96	42

As the results in Table 18 show, triethylamine promoted platinised Raney Nickel to a considerable extent, and Raney

Nickel itself to a slight extent. Trimethylamine promoted the platinised catalyst slightly. In all other cases retardation was obtained. The addition of sodium hydroxide overcame the retardation and with the platinised catalyst gave a pronounced promotion of the hydrogenation.

Tetraethyl ammonium hydroxide was found to give a promotion effect almost equivalent to that of sodium hydroxide in the hydrogenation of methyl ethyl ketone (1 g. ketone in 20 ml. ethanol), using platinised Raney Nickel.

Table 19

Comparison of the promotion effects of NaOH and tetraethylammonium hydroxide

Promoter	Amount of promoter added to 0.5 g. Ptsed R. Ni.	Rate of hydrogen absorption. Time of 10 ml. absorption (secs.)
NaOH	0.12 ml. 10 N soln.	65
$Et_4N.OH$	0.1 ml. 25% soln.	70

Addition of trimethylbenzyl ammonium hydroxide to the hydrogenation system of methyl ethyl ketone (1.0 g), platinised Raney Nickel (0.5 g.) and ethanol (20 ml.) coincided with a sudden rise in the rate of hydrogen absorption followed by as sudden a fall to a rate substantially lower than that prior to the addition of the hydroxide. Further investigation of this phenomenon - 7.6 ml. of the hydroxide solution

(= 0.017 g. mole.) was shaken with Raney Nickel (1 g.) in ethanol (20 ml.) in an atmosphere of hydrogen to give an uptake of hydrogen of 1 mole. per mole. of hydroxide - indicated that hydrogenolysis occurred to give toluene (b 109-110°, n_D^{19} 1.4970) and trimethylamine. This result is in agreement with those of Emde and Kull (69), for the hydrogenolysis of quaternary ammonium compounds with platinum catalyst. As an extension of this effect the hydrogenation of N-methylpyridinium hydroxide was studied.

Preparation of N-methyl pyridinium iodide (70).

Anhydrous pyridine (15 ml.) purefied via the zinc chloride complex (71) was reacted with methyl iodide (12 ml.) which was added slowly with cooling. After ½ hr., the resulting crystalline mass was warmed on a water bath, more methyl iodide being added until the odour of pyridine disappeared. Excess methyl iodide was evaporated off. The N-methyl pyridinium iodide was recrystallised twice from ethanol; m. 117° C.

Preparation of N-methyl pyridinium hydroxide.

Freshly precipitated silver oxide was prepared by reacting a solution of $AgNO_3$ (26.5 g. in 100 ml H_2O) with KOH (8.75 g. in 100 ml H_2O). The precipitated oxide was filtered off and washed with distilled water. It was added

to a solution of N-methyl pyridinium iodide (31.4 g.) in 100 ml. H_2O, and the mixture was stirred rapidly for ten minutes under nitrogen to prevent absorption of carbon dioxide. The solution of N-methyl pyridinium hydroxide was then filtered free of silver iodide and estimated by titration with standard HCl.

Hydrogenation of N-methyl pyridinium hydroxide.

A solution of N-methyl pyridinium hydroxide (0.095 mole.) in water (200 ml.) was hydrogenated at 45 p.s.i. hydrogen pressure over 5 g. Raney Nickel catalyst. Approximately 3 moles. of hydrogen were absorbed. After filtering off the catalyst the solution was saturated with potassium carbonate and extracted with ether (3 x 100 ml.). The ether extract was dried over $MgSO_4$. The ether was distilled off and the residue was distilled to give two amine fractions.

(1) b_{750} 100-105°, 20% yield, identified as N-methyl-piperidine by comparison with an authentic specimen; picrate d.228°.

(2) a basic fraction b_{15} 140-1°, 56% yield; analysis C 73.2, H 12.3, N 14.2, M.W. 195.

The second fraction was found to be a tertiary base which was readily soluble in water and extremely hygroscopic. It would appear to be identical with 1:1^1-dimethyl-4:4^1-dipiperidyl (C 73.4, H 12.3, N 14.3, M.W. 196) which was obtained by

Ochiai and Kataoka (52) by electrolytic reduction of N-methylpyridinium methosulphate. It gave a picrate (C 44.0, H 4.9, N 16.7; calc. C 44.0, H 4.6, N 17.1) which decomposed at 220° (cf. Ochiai and Kataoka, d. 225°).

Hydrogenation of N-methyl pyridinium iodide.

N-methyl pyridinium iodide (11.1 g.) in water (40 ml.) was hydrogenated at 45 p.s.i. hydrogen pressure over 5 g. Raney Nickel catalyst. When the product was worked up, N-methyl piperidine was obtained in 62% yield and 1:1'-dimethyl-4:4'-dipiperidyl in 10% yield. Barltrop and Taylor (47), obtained N-methylpiperidine in 90% yield by hydrogenating quaternary salts of pyridine in ethanol over Raney Nickel in the presence of diethylamine at 140° and 60 ats. hydrogen pressure. Other investigators (48,49,50, 51), studied the catalytic reduction of substituted pyridinium salts and reported the production of the corresponding piperidine.

Promotion of the hydrogenation of ketones over Raney Nickel catalyst.

In comparing various methods of promotion of Raney Nickel in the hydrogenation of ketones, the standard scheme adopted was the determination of the time of hydrogenation of 0.01 g. mole of ketone over 0.5 g. Raney Nickel in 20 ml. ethanol at atmospheric hydrogen pressure. The following catalyst

systems were studied:-

(a) 0.5 g. Raney Nickel,

(b) 0.5 g. Raney Nickel + 1.2 m. moles NaOH (as a 10N aqueous solution),

(c) 0.5 g. Raney Nickel + 0.33 ml. Et_3N,

(d) 0.5 g. Platinised Raney Nickel + 1.2 m. moles NaOH, (Delépine's promotion method (38),),

(e) 0.5 g. Platinised Raney Nickel + 0.12 m. moles NaOH + 0.33 ml. Et_3N,

(f) 0.5 g. Raney Nickel + 0.33 ml. Et_3N + 0.037 m. moles H_2PtCl_6 (Lieber's method (45)),

(g) 0.5 g. Raney Nickel + 0.33 ml. Et_3N + 0.037 m. moles H_2PtCl_6 + 1.2 m. moles NaOH.

With the cyclopentanones, 0.05 mole. of ketone was hydrogenated over 2.0 g. Raney Nickel and the quantities of promoters were increased proportionately.

The various promotion methods were also studied in hydrogenations at 45 p.s.i. differential hydrogen pressure, using 3 g. Raney Nickel with 0.05 g. mole of ketone in 40 ml. ethanol. In this case the catalyst systems studied were:-

(a) 3 g. Raney Nickel,

(b) 3 g. Platinised Raney Nickel + 6.0 m. moles NaOH,

(c) 3 g. Raney Nickel + 2 ml. Et_3N + 0.22 m. moles H_2PtCl_6,

(d) 3 g. Raney Nickel + 2 ml. Et_3N + 0.22 m. moles H_2PtCl_6 + 6.0 m. moles NaOH.

As an example, the results obtained for acetone are given in detail below.

Table 20

Hydrogenation of Acetone at Atmospheric Pressure

Hydrogenation System	Vol. of H_2 absorbed (mls)	Time for absorption (mins)	Hydrogenation System	Vol. of H_2 absorbed (mls)	Time for absorption (mins)
a) R.Ni. (0.5g)	50	7	b) 0.5 g.R.Ni + 1.2 m.mole. NaOH	50	3.9
	100	13.6		100	7.9
	150	20.3		150	11.9
	200	28.8		200	16.9
	220	34.3		220	19.9
	230	39.3		230	23.4
c) 0.5 g.R.Ni + 0.33 ml Et_3N	50	4.3			
	100	9.4			
	150	14.9			
	200	21.2			
	230	27			
	240	31			
d) 0.5 g Ptsed R.Ni + 1.2 m.mole NaOH	50	3.9	e) 0.5 g Ptsed R.Ni + 1.2 m. mole NaOH + 0.33 ml Et_3N	50	5
	100	8.2		100	10.25
	150	12.4		150	15.5
	200	17.5		200	23.25
	220	19		220	25.4
	230	21		230	28.4

Hydrogenation System	Vol. of H_2 absorbed (mls)	Time for absorption (mins)	Hydrogenation System	Vol. of H_2 absorbed (mls)	Time for absorption (mins)
f) 0.5 g.R.Ni. + 0.33 ml Et_3N + 0.037 m. mole H_2PtCl_6	50	3.25	g) As in (f) + 1.2 m.mole NaOH	50	2.5
	100	6.6		100	5.1
	150	9.9		150	7.75
	200	14.3		200	10.5
	230	20		220	13.1
	240	25		230	16

Table 21

Hydrogenation of Acetone at 45 p.s.i. hydrogen pressure

Hydrogenation System	Fall in H_2 Pressure (lbs.)	Time (mins)	Hydrogenation System	Fall in H_2 Pressure (lbs.)	Time (mins)
a) 3 g.R.Ni.	1.0	2	b) 3 g. Ptsed R.Ni + 6.0 m. mole NaOH	0.8	1
	2.0	4.5		1.8	2
	3.0	7		2.8	2.75
	4.0	10		3.8	4
	4.8	13		4.8	5
				5.0	7.5
c) 3 g.R.Ni + 2 ml Et_3N + 0.22 m.mole H_2PtCl_6	1.4	1	d) As in (c) + 6.0 m.mole NaOH.	1.2	0.75
	2.4	2		2.2	1.5
	3.4	3		3.2	2.25
	4.4	4		4.2	3.0
	5.0	7		5.0	4.5

Recovery and identification of the alcohol product of hydrogenation of ketones.

After completion of hydrogenation, the solution of the hydrogenation product in ethanol was filtered free from Raney Nickel catalyst which was then washed with 6 x 15 ml. ethanol. A little hydrochloric acid was added to neutralise any free alkali. The ethanol was removed by distillation under reduced pressure through a six inch bead packed column. The last few ml. of ethanol was removed by azeotropic distillation with benzene. The column was washed out with benzene and the benzene solution of the hydrogenation product was washed with water (10 ml.) to remove any inorganic

material. The water was in turn extracted with benzene (20 ml.). The combined benzene extracts were dried ($MgSO_4$), benzene was removed by distillation, and finally the residue was distilled. The recovery of the alcohol product varied from c.80% for the more volatile to c.95% for the high-boiling less volatile alcohols. They were identified as 3:5 dinitrobenzoates (72). In those cases where the 3:5 dinitrobenzoate was not listed in the literature, a nitrogen analysis was done in order to confirm its composition (table 22).

Table 22

3:5 dinitrobenzoates of certain alcohols

Alcohol	3:5-dinitrobenzoate		
	m.p.	Nitrogen analysis	
		Found.	Calc.
3-heptanol	54-55	9.20	9.03
ethyl phenyl carbinol	69-70	8.60	8.49
2:2-dimethylcyclohexanol	106-107	8.52	8.70
2:2:6:6-tetramethylcyclohexanol	158-159	7.91	8.00
2:2-dimethylcyclopentanol	70.5-72	9.13	9.09

Comparison of the ageing of Raney Nickel and Raney Nickel-Platinum catalysts.

The effect of ageing upon the activity of Raney Nickel prepared from an alloy of 49% Ni, 49% Al and 2% platinum was

found by measuring the time for hydrogenation of acetone (0.01 mole.) in ethanol (20 ml.) over 0.5 g. of catalyst, and over 0.5 g. catalyst promoted with 1.2 m. mole. NaOH. The results in table 23 are compared with those for standard Raney Nickel taken from table 17.

Table 23

Comparison of the ageing of Raney Nickel and Raney Nickel Platinum catalyst.

Raney Nickel			Raney Ni-Pt.		
No. of days after preparation of catalyst	Time for hydrogenation over R.Ni. $t_{1.0}$(mins)	Time for hydrogenation over R.Ni. + NaOH ($t_{1.0}$(mins)	No. of days after preparation of catalyst	Time for hydrogenation over R.Ni-Pt $t_{1.0}$(mins)	Time for hydrogenation over R.Ni-Pt. + NaOH $t_{1.0}$(mins)
2	19	15	2	18	12
10	25	17	22	21	15
34	34	19			

The results indicated that the Ni-Pt alloy catalyst retained much of its initial activity for a longer time than Raney Nickel catalyst.

Adsorption of sodium hydroxide by Raney Nickel catalyst.

6.0 m. mole NaOH (equiv. to 59.4 ml 0.1017 N HCl) was added to 3 g. Raney Nickel in 40 ml EtOH, and shaken up in an atmosphere of hydrogen for ten minutes. The ethanol

was filtered off, and evaporated down; water was added and the solution titrated with HCl solution. Titre - 19.2 ml.

The experiment was repeated, the ethanol was filtered off, and the catalyst washed with 6-15 ml lots of ethanol. The ethanol was evaporated down and water added, titration with HCl gave the following titre - 31.9 ml. These results indicated that the sodium hydroxide was strongly adsorbed on the catalyst surface.

Comparison of LiOH and NaOH as promoters of Raney Nickel Catalyst.

0.01 g. mole. of various ketones was hydrogenated with 0.5 g. catalyst, unpromoted and promoted with NaOH (1.2 m. mole.) and with LiOH (0.3 m. mole.). The results of table 24 indicated that LiOH was about 20% more efficient than NaOH as a promoter.

Table 24

Comparison of the promotion effects of LiOH and NaOH

Ketone	Time of hydrogenation (mins.)		
	R. Ni. (unpromoted)	R. Ni. promoted by NaOH	R. Ni. promoted by LiOH
Acetone	39	31	25
Methyl ethyl	54	35	30
methyl n-propyl	70	41	34
methyl n-butyl	81	60	42

Promotion of adsorption of hydrogen on Raney Nickel catalyst by sodium hydroxide.

Raney Nickel catalyst (3.0 g.) in ethanol was shaken in an atmosphere of hydrogen until no further absorption of hydrogen occurred. On adding 3.0 m. mole. NaOH, further absorption of Hydrogen was observed (table 25).

Table 25

Promotion of adsorption of hydrogen on Raney Nickel by NaOH

Age of Raney Nickel catalyst	Adsorption of hydrogen (ml.) after addition of 3.0 m.mole NaOH
4 hrs.	14.8
24 days	14.1

Hydrogenation of cyclohexene.

Cyclohexene (0.01 mole.) in ethanol (20 ml.) was hydrogenated over a) 0.5 g. Raney Nickel catalyst, and b) 0.5 g. catalyst to which 0.3 m. mole NaOH had been added. The course of hydrogenation is given in table 26.

Table 26

Hydrogenation of cyclohexene

a)	Hydrogen absorption (ml.)	Time (mins.)	b)	Hydrogen absorption (ml.)	Time (mins.)
	50	2.4		50	2.3
	100	4.7		100	4.7
	150	6.9		150	7.2
	200	9.4		200	9.9
	210	10.0		210	11.0
	220	12.0		220	14.0

The results indicated that sodium hydroxide retarded the reaction.

Hydrogenation of nitrobenzene.

Nitrobenzene (0.5 g.) was hydrogenated similarly. The course of hydrogenation is given in table 27.

Table 27

Hydrogenation of nitrobenzene

a)	Hydrogen absorption (ml.)	Time (mins.)	b)	Hydrogen absorption (ml.)	Time (mins.)
	50	3.3		50	3.0
	100	6.25		100	6.25
	150	9.6		150	9.0
	200	12.9		200	12.25
	250	16.3		250	15.75
	300	20.3		300	18.5
	350	29		340	26.0

It was found that although sodium hydroxide had no effect on the initial rate, it gave a sharper completion of the reaction.

Effect of amount of NaOH on the promotion of Raney Nickel in the hydrogenation of acetone.

Acetone (0.01 mole) was hydrogenated over Raney Nickel (0.5 g.) in ethanol (20 ml.) to which sodium hydroxide solution (0.1 ml.) had been added. The promotion effect caused by sodium hydroxide solutions of increasing strength was found by measuring the time of hydrogenation. The results are given in table 28.

Table 28
Effect of amount of NaOH on the promotion Raney Nickel.

Normality of NaOH solution	Time of hydrogenation (mins.)	Normality of NaOH solution	Time of hydrogenation (mins.)
0	43;42	2	25
0.1	39	2.25	25
0.25	34	2.5	26
0.5	30	3	25
0.75	30;29	4	26
1.0	26;27	5	27;28
1.25	26	7	30
1.5	26	9	32,31
1.75	26		

BIBLIOGRAPHY

(1) Lennard-Jones, Trans. Far. Soc., 1932, 28, 334.

(2) Trapnell, Quart. Revs., 1954, VIII, 404.

(3) Beeck, Smith and Wheeler, Proc. Roy. Soc., 1940, 177A, 62.
Beeck and Ritchie, Discuss. Far. Soc., 1950, 8, 118.

(4) Dowden, Research 1948, 1, 239.

(5) Dowden, J. C. S., 1950, 242.

(6) Dilke, Maxted & Eley, Nature, 1948, 161, 804.

(7) Couper and Eley, Discuss. Far. Soc., 1950, 8, 172.

(8) Dowden and Reynolds, ibid, 184.
Reynolds, J. C. S., 1950, 265.

(9) Moore and Selwood, J.A.C.S. 1956, 78, 697.

(10) H. S. Taylor, Proc. Roy. Soc., 1925, 108A, 105.

(11) Maxted, J.C.S. 1922, 1760.
ibid., 1925, 73.
ibid., 1928, 1600.
ibid., 1933, 502.
ibid., 1934, 26, 672.

(12) Herington and Rideal, Trans. Far. Soc., 1944, 40, 505.

(13) Boudart, J.A.C.S., 1952, 74, 3556.

(14) Baker and Rideal, Nature, 1954, 174, 1185.

(15) Bond, Quart. Revs. 1954, VIII, 280.

(16) Turkevich, Schissler & Irsa, J. Phys. Chem., 1951, 55, 1078.

(17) Twigg, Discuss. Far. Soc., 1950, 8, 152.

(18) Farkas, Farkas and Rideal, Proc. Roy. Soc., 1934, 146A, 630.

(19) Twigg and Rideal, ibid., 1939, 171A, 55.

(20) Jenkins and Rideal, J.C.S., 1955, 2490, 2496.

(21) Farkas and Farkas, J.A.C.S., 1939, 61, 1336.

(22) Anderson and MacNaughton, ibid., 1942, 64, 1459.

(23) Freidman and Turkevich, ibid., 1952, 74, 1669.

(24) Murray Raney, U.S.P. 1,628,190 (1927).

(25) Covert and Adkins, J.A.C.S., 1932, 54, 4116.

(26) Adkins and Pavlic, ibid., 1946, 68, 1471.

(27) Adkins and Billica, ibid., 1948, 70, 695.

(28) Baker and Adkins, ibid., 1940, 62, 3305.

(29) Kleiderer and Cornfield, J.Org.Chem., 1948, 13, 455.

(30) Prelog et al., Helv. Chim. Acta, 1946, 29, 360.
Grigorovskiĭ and Federov, Chem. Abs., 1949, 43, 646.

(31) Mozingo, J.A.C.S., 1946, 65, 1013.

(32) Taylor and Weiss, Nature, 1938, 141, 1055.

(33) Ipatieff and Pines, J.A.C.S., 1950, 72, 5320.

(34) Watt and Parker, ibid., 1952, 74, 1103.

(35) H. A. Smith, Chadwell and Kirslis, J.Phys.Chem., 1955, 59, 820.

(36) Freĭdlin and Ziminova, Chem. Abs., 1951, 45, 6029.

(37) Pattison and Degering, J.A.C.S., 1951, 73, 486.

(38) Delépine and Horeau, Bull. soc. chim., 1937, 4, 31.

(39) Lieber et al., J.A.C.S., 1936, 58, 1417.
ibid., 1939, 61, 384.
ibid., 1941, 63, 1192.

(40) Paty, Compt. rend., 1945, 220, 828.

(41) Fluchaire and Chambret, Bull. soc. chim., 1944, 11, 22.

(42) Décombe, Compt. rend., 1946, 222, 90.

(43) Heilmann, Dubois and Beregi, ibid., 223, 737.

(44) J. W. Skelly, Glasgow Univ. Hons. B.Sc. Thesis, 1949.

(45) Lieber et al., J.A.C.S., 1950, 72, 1191.

(46) Samuelson, Garik and Smith, ibid., 3872.

(47) Barltrop and Taylor, J.C.S., 1951, 108.

(48) Harris, Shelton, Van Campen and Schumann, J.A.C.S., 1951, 73, 3965.

(49) Phillips, ibid., 1950, 72, 1850.

(50) Truitt, Hall and Arnwine, ibid., 1952, 74, 4552.

(51) Lukeš, Kovář and Blaha, Chem. listy. 1956, 50, 264.

(52) Ochiai and Kataoka, Chem. Abstr., 1951, 45, 5150e.

(53) Pattison and Degering, J.A.C.S. 1951, 73, 611.

(54) Cornubert and Réal, Bull. soc. chim., 1952, 19, 407. Cornubert and Kazig, ibid., 410.

(55) Griffith, Trans. Far. Soc., 1937, 33, 407.

(56) Dupont and Piganiol, Bull. soc. chim., 1939, 6, 322.

(57) Cornubert and Phélisse, ibid., 1952, 19, 403.

(58) O. Schmidt, Z. phys. Chem., 1936, A176, 254.

(59) Bremner and Keeys, J.C.S., 1947, 1068

(60) E. Guenther, "Essential Oils", 1949, Vol. II, p. 418.

(61) Zelinsky and Pavlow, Ber. 1924, 57, 1066; 1925, 58, 185.

(62) Vogel, "Practical Organic Chemistry", 1954, 338.

(63) Vogel, J.C.S., 1931, 907.

(64) Cornubert and Borrel, Bull. soc. chim., 1930, 47, 301.

(65) Haller and Cornubert, ibid., 1926, 39, 1724.

(66) Willstätter and Jacquet, Ber., 1918, 51, 761.
Willstätter and Waldschmidt-Leitz, ibid., 1920, 54, 113.

(67) Carothers and Adams, J.A.C.S., 1923, 45, 1071; 1924, 46, 1675.

(68) H. A. Smith and Fuzek, ibid., 1948, 70, 3743.

(69) Emde and Kull, Chem. Abs. 1936, 30, 2932, 4824.

(70) Cumming, Hopper and Wheeler, "Systematic Organic Chemistry", 1937, p. 244.

(71) Vogel, "Practical Organic Chemistry", 1954, p. 174.

(72) Hopkins and Williams Ltd., "Organic Reagents for Organic Analysis", 1944, p. 48.

(73) Bond, Trans. Far. Soc., 1956, 52, 1235.

(74) Flanagan and Rabinovitch, J. Phys. Chem., 1956, 60, 724.

(75) Cranstoun, Glasgow Univ. Hons. B.Sc. Thesis, 1955.

Preprinted from the Journal of the Chemical Society, July, 1954, (5206), pages 2487—2489.

The Promotion of Raney Nickel Catalysts.

By ROBERT B. BLANCE and DAVID T. GIBSON.

[Reprint Order No. 5206.]

Delépine has shown that in the hydrogenation of ketones, Raney nickel is promoted by treatment with chloroplatinic acid followed by sodium hydroxide. Lieber has shown that treatment with triethylamine and chloroplatinic acid is also effective. We find that a combination of the two techniques is better than either, and that lithium hydroxide can, with advantage, replace sodium hydroxide.

IN addition to successive improvements (Adkins, *J. Amer. Chem. Soc.*, 1948, **70**, 695) in the preparation of Raney nickel catalysts it has been shown that for many reductions the catalyst is promoted by treatment with sodium hydroxide, chloroplatinic acid, triethylamine, etc. Delépine and Horeau (*Bull. Soc. chim.*, 1937, **4**, 31) found that Raney nickel platinised with chloroplatinic acid solution was substantially promoted for reduction of the carbonyl group, but not of double bonds, by treatment with a little aqueous sodium hydroxide. Lieber and Smith (*J. Amer. Chem. Soc.*, 1936, **58**, 1417) added to Raney nickel triethylamine followed by chloroplatinic acid solution. The sparingly soluble triethylamine chloroplatinate deposited platinum on the catalyst, so that the platinising is probably more uniform than by direct addition of chloroplatinic acid to the nickel suspension, for then the first particles to encounter the solution would be overplatinised and the remainder unplatinised. The possibility of uneven platinising is confirmed by Delépine and Horeau's observation (*loc. cit.*) that whereas Raney nickel dissolves completely in dilute acid, platinised Raney nickel always leaves a small nickel-containing residue. Heilman, Dubois, and Beregi (*Compt. rend.*, 1946, **223**, 737), using Raney nickel W1, reported the superiority

TABLE 1. *Time (minutes) for hydrogenation of ketones. Promotor for the Raney nickel catalyst.*

Ketone	None	NaOH	Et_3N	Pt + NaOH	Et_3N + Pt	Et_3N + Pt + NaOH
			Reaction at 1 atm.			
Dimethyl	39	24	31	21	25	16
Ethyl methyl	52	38	47	27	47	19
Methyl *n*-propyl	76	36	64	30	83	21
Methyl *n*-pentyl	77	57	83	33	93	25
*iso*Butyl methyl	78	53	—	35	126	27
Diethyl	80	—	—	37	221	27
n-Butyl ethyl	82	—	—	38	265	34
Di*iso*propyl	*i*	—	—	253	*x*	*i*
*cyclo*Hexanone	40	40	—	21	37	17
4-Methyl*cyclo*hexanone	60	45	—	23	36	20
2-Methyl*cyclo*hexanone	88	65	—	45	161	32
2 : 2-Dimethyl*cyclo*hexanone	93	70	—	49	167	32
2 : 2 : 6-Trimethyl*cyclo*hexanone	472	—	—	264	*i*	200
2 : 2 : 6 : 6-Tetramethyl*cyclo*hexanone	*i*	—	—	1600	—	1600
Camphor	580	—	—	329	—	153
Acetophenone	57	30	38	19	15	14
Propiophenone	90	55	65	34	24	24
Benzophenone	70	40	39	38	34	16
			Reaction at 3 atm.			
3-Methyl*cyclo*hexanone	24	—	—	11·5	15	9
4-Methyl*cyclo*hexanone	24	—	—	11	15	9
Fenchone	—	—	—	*i*	—	720

i = incomplete reaction; *x* = no absorption of hydrogen.

of Delépine's method "sur un grand nombre d'autres composées à fonction carbonyle." We compared the two methods for the reduction of ketones by using Raney nickel W4, and we found that for aliphatic and alicyclic ketones Delépine's method was superior, but that with some aromatic ketones, Lieber's method was slightly better. Further, we found that in all cases a combination of the two techniques, *i.e.*, platinising the catalyst by using triethylamine (Lieber), followed by addition of sodium hydroxide (Delépine), was superior to either. The rates of hydrogenation at 1 and at 3 atmospheres pressure were invariably increased, usually by as much as 20%. Table 1 shows that while Lieber's catalyst is fairly efficient for acetone and *cyclo*hexanone, its performance is considerably poorer for higher ketones. Sodium hydroxide, however, extends the range of efficiency and also retards the ageing of the catalyst.

The promoted catalyst (0·5 g.), ethanol (20 ml.), the ketone (10 mmoles), and 10N-sodium hydroxide (1—2 mmoles) were shaken with hydrogen at 200 double strokes per minute. The best results were obtained with a catalyst promoted by adding triethylamine (3·3 mmoles), chloroplatinic acid (0·04 mmoles) and finally 10N-sodium hydroxide (1·2 mmoles) to a rapidly stirred suspension of Raney nickel catalyst (0·5 g.). The catalyst was then washed three times with distilled water and three times with alcohol. Ketones and solvent were left overnight in contact with Raney nickel to remove poisons and were filtered and redistilled. The Raney nickel catalyst was prepared from Murex 50% nickel–aluminium Alloy (80 to dust) by Adkin's and Pavlic's method (*J. Amer. Chem. Soc.*, 1946, **68**, 1471) for Raney nickel catalyst W4.

Since Patterson and Degering (*J. Amer. Chem. Soc.*, 1951, **73**, 611) have reported poisoning of Raney nickel by chloride ion, we avoided the use of chloroplatinic acid by preparing the catalyst from a specially made aluminium–nickel alloy containing 2% of platinum. Table 2 shows that this catalyst is not only better than the unpromoted catalyst, but is at least as efficient and much easier to use than our promoted catalyst for the more difficult hydrogenations.

TABLE 2. *Times of hydrogenation of ketones with Raney nickel catalysts perpared from* Ni–Al *containing* 2% *of platinum.*

	Un-promoted	Promoted by NaOH		Un-promoted	Promoted by NaOH
Dimethyl ketone	41	23	2 : 2′ : 6-Trimethyl*cyclo*-hexanone	352	159
*cyclo*Hexanone	40	27	(+)-Camphor	273	155
2-Methyl*cyclo*hexanone ...	54	28			

Since the completion of these experiments, Cornubert and Phélisse (*Bull. Soc. chim.*, 1952, **19**, 403) have confirmed that Raney nickel is poisoned by chloride ion, but showed that at a chlorine : catalyst ratio of 1 : 100 the effect is scarcely detectable. As we had used 1 mole of chloroplatinic acid per 500 moles of catalyst, it is evident that even if *none* of the liberated chloride had been removed in the subsequent washing, its effect on the catalyst would have been negligible.

The promoting effect of sodium hydroxide has been ascribed by Dupont and Piganiol (*ibid.*, 1939, **6**, 322) to localised adsorption of ketone on areas containing adsorbed sodium ions. Assuming that the hydrogen is adsorbed on areas free from sodium, they postulated that reaction takes place at the boundaries. While their view may account for the existence of an optimum amount of sodium hydroxide (which we found to be 0·4 mmole per g. of catalyst)(cf. Cornubert and Kaziz, *ibid.*, 1952, **19**, 410) it suggests that sodium hydroxide should, in the absence of an acceptor, diminish the amount of hydrogen taken up by Raney nickel. Actually, we found that addition of sodium hydroxide caused adsorption of an additional 5 ml. of hydrogen per g. of nickel. Our results are more in harmony with Bremner and Keey's views (*J.*, 1947, 1079) that the catalyst may be regarded as an electron donor or acceptor, and that addition of electropositive ions to it will tend to increase its electron-donor characteristics, so that alcohol will tend to be desorbed. The increased rate of hydrogenation of carbonyl compounds following the addition of alkali may therefore be due to an increase in the catalyst area made available by the more rapid desorption of the alcohol resulting from the reduction.

In a study of the catalytic reduction of ethylenes in solution in various alcohols, Schmidt (*Z. physikal. Chem.*, 1936, *A*, **176**, 254) considered that a measure of the relative affinities of the solvent and of the ethylene for the catalyst surface was given by the ratio of their heats

of vaporisation. Thus, where the ratio was large, reaction was slow because of a preferential adsorption of solvent molecules on the surface, tending to prevent access of ethylene.

A similar correspondence was noted in the present work; the activity of the catalyst was enhanced by the presence of sodium hydroxide in cases where the heat of vaporisation of the product is substantially greater than that of the original ketone. This is confirmed by the results of Samuelson, Garik, and Smith (*J. Amer Chem. Soc.*, 1950, **72**, 3872) for the majority of simple nitro-compounds examined. On the other hand the ratio of the heats of vaporisation of *cyclo*hexene and *cyclo*hexane is nearly unity and addition of sodium hydroxide slightly retards reaction. Some of these results are collected in Table 3.

TABLE 3.

Substrate	Heat of vaporisation, kcal. mole^{-1}	Reduction product	Heat of vaporisation, kcal. mole^{-1}	Effect of NaOH
Acetone	7·26	2-Propanol	9·56	Promotes
Ethyl methyl ketone	7·59	2-Butanol	9·92	,,
*cyclo*Hexanone	9·50	*cyclo*Hexanol	10·70	,,
Nitrobenzene	7·94	Aniline	9·91	,,
*cyclo*Hexene	7·28	*cyclo*Hexane	7·34	Retards

Cornubert and Phélisse (*loc. cit.*) demonstrated elegantly the selective character of promotion by sodium hydroxide by showing that in its absence unsaturated ketones were rapidly and sharply converted into saturated ketones, and that thereafter the reduction could be continued to give the saturated alcohol by adding sodium hydroxide.

The similarity between the ionic radii of lithium and of nickel suggested that if promotion is due to adsorption of sodium ions lithium hydroxide might function better. The results in Table 4 show that lithium hydroxide is about 20% better than sodium hydroxide. Optimum results are obtained by using 0·6 mmole of lithium hydroxide per g. of Raney nickel.

TABLE 4. *Times for hydrogenation of ketones with Raney nickel and alkali.*

Ketone	Unpromoted	Promoted by NaOH	Promoted by LiOH	Ketone	Unpromoted	Promoted by NaOH	Promoted by LiOH
Dimethyl	39	31	25	Methyl *n*-propyl	70	41	34
Ethyl methyl	54	35	30	*n*-Butyl methyl	81	60	42

Potassium hydroxide was a less efficient promoter than sodium hydroxide for reduction of ethyl methyl ketone (1·17 : 1) and *n*-butyl methyl ketone (1·33 : 1).

The authors thank the Mond Nickel Co. for the loan of diffusion apparatus, Messrs. Murex for making special alloys containing platinum, Messrs. Glaxo for a gift of ketones, and Mr. Steele for assistance with the lithium hydroxide experiments.

UNIVERSITY OF GLASGOW. [*Received, March 12th*, 1954.]

PRINTED IN GREAT BRITAIN BY RICHARD CLAY AND COMPANY, LTD.,
BUNGAY, SUFFOLK.

PART II.

THE STEREOCHEMISTRY OF CATALYTIC HYDROGENATION OF CYCLIC KETONES

I N D E X

S U M M A R Y

Promotion of Raney Nickel catalyst in the hydrogenation of substituted cyclopentanones and cyclohexanones has been found to give a slight but not significant increase in the amount of the thermodynamically less stable isomeric alcohol.

The reduction of methylcyclopentanones by catalytic and chemical methods has been studied. Reduction of (±)-2-methylcyclopentanone conformed with Barton's generalisations for reduction of cyclic ketones. The proportion of isomers produced from (±)-3-methylcyclopentanone, however, was unaffected by the method of reduction; one isomer predominated in every case and was assigned the cis configuration on the basis of studies of the reduction of 3-methylcyclopent-2-en-1-one and of (±)-3-methylcyclopent-2-en-1-ol.

Studies of the equilibration of isomeric cyclohexanols at a catalyst surface showed that the ratio of isomers produced by hydrogenation of cyclic ketones was not related to a thermodynamically reversible reaction. It was concluded that the catalytic hydrogenation of ketones could best be interpreted in terms of a broadside-on mechanism of adsorption of the ketone molecule followed by addition of hydrogen from the direction of the catalyst.

INTRODUCTION

It has long been known that when reduction of organic substances can give rise to geometric isomers, then the ratio of the isomers is profoundly affected by the reducing agent and by the reaction conditions. From a study of the reduction of unsaturated substances, Skita (1), in 1923 suggested that the cis isomer is produced by reduction in acid solution and the trans isomer by reduction in neutral or alkaline solution. Together with the von Auwers' rule (2), which stated that of two isomers, the cis is denser, has greater index of refraction and lower molecular refraction than the trans, Skita's rule became a classical method for assigning configuration. This in spite of the fact that von Auwers (3), had questioned its validity, maintaining that Skita's conclusions were based on incompletely separated mixtures of isomers. Later when Skita observed that catalytic hydrogenation of 2-methylcyclohexanone was promoted by organic bases to give an increase in the amount of cis isomer (53%) compared with hydrogenation in neutral solution (35%), he modified his rule (4), to state that the greater the rate of hydrogenation then the greater is the amount of less stable isomer produced.

Vavon (5), studied the reduction of cyclic ketones extensively and from his results he proposed that production of the cis isomer is favoured in catalytic hydrogenation

over platinum, and production of the trans isomer is favoured by reduction with sodium and alcohol, the composition of the mixture obtained in the latter case being the same as is obtained by direct equilibration, (6). In a study of the reduction of cholestanone (7), he showed that catalytic hydrogenation must be accomplised in acid medium in order to ensure the predominant formation of the cis isomer, a result which was confirmed by Ruzicka et al. (8), in the hydrogenation of coprostanone. Vavon (7), also demonstrated that the amount of epicholestanol produced in the hydrogenation of cholestanone with platinum in acid solution varied from 65-95% of the epimeric mixture according to the activity of the catalyst. Vavon's generalisation was confirmed by Anziani and Cornubert (9), in the hydrogenation of 2-methyl-cyclohexanone and by Claudon (10), in the hydrogenation of 3- and 4-methyl-cyclohexanones. Anziani and Cornubert (9), found that there was no correlation between the rate of hydrogenation over platinum black and the amount of cis isomer formed; they observed that addition of hydrochloric acid to the catalyst seemed to have a specific directing effect yielding the cis isomer almost exclusively.

The reduction of cyclohexanones by other methods has been studied. Macbeth et al. (11), investigated the Meerwein-Ponndorf-Verley reduction with aluminium isopropoxide. They

found that the proportion of cis isomer in the product was greatest for those ketones in which steric hindrance was greatest and that the proportion of cis isomer produced from menthone was increased by using bulkier aluminium alkoxides. Noyce et al. (12), observed that reduction with lithium aluminium hydride normally gave a preponderance of trans isomer, although in some cases the proportion of cis isomer was markedly higher than that obtained by reduction with sodium and alcohol and indeed with sterically hindered ketones such as camphor, the cis isomer was formed almost exclusively.

In recent times, it has been demonstrated that molecules exist in preferred conformations, i.e. arrangements in space of the atoms of the molecule which are not superposable upon each other (13). It has been shown that the chair conformation of cyclohexane is more stable than the boat (14). The C-H bonds of the chair conformation are of two geometrically different types; six of the bonds lie parallel to the threefold symmetry axis of the ring and have been designated axial, the other six radiate out from the ring and have been termed equatorial (15). Studies on the electron diffraction of cyclohexane derivatives in the vapour phase (16), have shown that a substituted cyclohexane normally exists predominantly in the chair conformation which has the maximum number of substituents equatorial. Moreover, with unsymmetrically

substituted cyclohexanes, the stereoisomer with the greatest number of equatorial substituents is the more stable. Thus trans - 1:2- and 1:4- disubstituted cyclohexanes in which both substituents can adopt the equatorial conformation are thermodynamically more stable than the corresponding cis derivatives in which one substituent is necessarily axial. Similarly a cis-1:3- disubstituted cyclohexane is more stable than the trans-1:3- isomer. This was demonstrated experimentally and has led to the reversal of configuration of 1:3- disubstituted cyclohexanes (17), and a consequent reversal of the von Auwers' rule for them. The rule has also been found to be ambiguous when applied to polycyclic systems and has therefore been modified to state that for substituted cyclohexanes the stereoisomer with the more axial substituents has a higher refractive index and density (18). Another modification (19), proposed that for isomeric cyclohexane (and tetrahydropyran) derivatives which are similarly substituted on corresponding ring carbon atoms, the refractive indices and densities are inversely related to conformational stability.

In a Tilden Lecture on the stereochemistry of cyclohexane derivatives, Barton (20), suggested the following generalisations, for the reduction of substituted cyclohexanones:-

(1) rapid hydrogenation (in acid medium) affords the axial alcohol; slow hydrogenation (in neutral solution) affords the equatorial alcohol if the ketone group is unhindered, the axial alcohol if it is strongly hindered;

(2) reduction of the ketone with sodium and an alcohol gives a mixture of alcohols of the same composition as is obtained by direct equilibration;

(3) reduction with sodium borohydride, or with lithium aluminium hydride affords the equatorial alcohol if the ketone group is unhindered; the axial epimer if it is hindered;

(4) Meerwein-Ponndorf-Verley reduction which is only applicable to relatively unhindered ketones gives a higher proportion of axial hydroxyl than do other methods with the exception of catalytic hydrogenation in acid medium.

A study of the reduction of 2-alkyl and 2-aryl cyclohexanones by Cornubert (21), provided further experimental confirmation of these generalisations. In particular, reduction with platinum in acid medium was found to give the axial epimer almost exclusively. Recent work by Wicker (22), however, contradicts Barton's first generalisation. Wicker found that equilibration of stereoisomeric cyclohexanols occurs over alkaline catalysts such as Raney Nickel, reduced

nickel and Adams' platinum catalyst. Assuming therefore that the low percentage of less stable isomer obtained by reduction in alkaline solution was due to this isomerisation, he studied the hydrogenation of a number of cyclohexanones. He found that acid and alkali had little effect on the reduction product of 2-methylcyclohexanone, cis-2-methyl-cyclohexanol being formed predominantly in both cases. However from 3-methyl, 4-methyl- and 3:3:5-trimethylcyclohexanones a greater proportion of the more stable isomer resulted by reduction in acid solution than in alkaline solution and indeed from 3-methyl- and 4-methyl- cyclohexanones the more stable isomer was formed preponderantly by reduction in acid solution. Such a result contradicts the Skita rule and Barton's first generalisation.

Dauben et al.(47), have compared the reduction of cholestanones by lithium aluminium hydride and by catalytic hydrogenation. From the results for catalytic hydrogenation taken from the literature, they suggest that Barton's generalisation re acid reduction is an over simplification since C_1- and C_{12}- ketones give exclusively the equatorial alcohol and C_7 ketones yield mainly the equatorial alcohol.

This observation may be extended to ketones such as camphor which gives the equatorial alcohol by catalytic reduction and the axial alcohol by reduction with sodium and

alcohol. Barton's generalisation might therefore be amended to state that catalytic hydrogenation in acid medium yields a preponderance of the sterically more hindered alcohol which is generally the axial alcohol except in cases similar to those above where angular methyl groups or carbon bridges add complicating steric effects.

The reduction of cyclopentanones has received less study than that of the cyclohexanones. In an investigation of the reduction of 2-ethyl- and 2-propyl- cyclopentanones, Vavon (23), found that the cis isomer was produced predominantly by catalytic hydrogenation over platinum black and the trans isomer by reduction with sodium and alcohol. Godchot and Bedos (24), obtained trans- 2-methylcyclopentanol from 2- methylcyclopentanone by catalytic hydrogenation and by reduction with sodium and alcohol. Huckel and Kindler (25), reduced 2-methylcyclopentanone with sodium and alcohol to obtain the trans isomer (3:5-dinitrobenzoate m. 64°) and hydrogenated the ketone over Adams' platinum catalyst in acid medium to produce predominantly the cis isomer (3:5-dinitrobenzoate m. 124°). Later Turner (26), in an investigation of the stereochemistry of peracid oxidation of ketones, showed that neither Godchot nor Huckel had isolated the pure isomers. His work indicated that the cis isomer had a 3:5-dinitrobenzoate m. 67° and the trans isomer had a 3:5-dinitrobenzoate m.

88°. Huckel and Sauerland (27), in a further study concurred with Turner; they found that reduction of 2- methylcyclopentanone with aluminium isopropoxide yielded a mixture containing 70% of the cis isomer. Umland and Jefraim (28), however have shown that the cis isomer described by Huckel and by Turner was in fact a mixture of 58% cis and 42% trans isomer. They prepared the pure cis isomer by acetolysis of the p- toluenesulphonate of trans-2-methylcyclopentanol under neutral conditions. Their cis isomer gave a 3:5- dinitrobenzoate m. 86°. By reduction of 2-methylcyclopentanone with lithium aluminium hydride, they obtained a mixture of isomers containing 25% cis. Phillips and Mentha (29), in a study of the reduction of 2-benzylcyclopentanone obtained preponderant formation of the trans isomer by reduction with lithium aluminium hydride and of the cis isomer by reduction with Adams' platinum catalyst in acid medium. Godchot and Cauquil (30), investigated the reduction of ± 3- methylcyclopentanone. Reduction with sodium and moist ether gave equal quantities of cis and trans isomers while catalytic hydrogenation over platinum in acetic acid gave a 50% yield of 3-methylcyclopentanol which was claimed to be chiefly cis.

In this section of this thesis, the effect of promotion of Raney Nickel on the proportion of isomers obtained by hydrogenation of substituted cyclopentanones and cyclohexanones

has been studied. The study of the reduction of methyl-cyclopentanones has been extended to include chemical methods of reduction and the proportion of isomers obtained by such methods has been determined.

G E N E R A L

Isolation and Analysis of the Epimeric Mixture.

When the hydrogenation of a cyclic ketone was complete, the catalyst was removed by filtration and then the ethanol was removed by distillation under reduced pressure through a fractionation column and finally by a distillation with benzene. The mixture of epimeric alcohols was distilled. The overall yield was approximately 90%; it was shown by spectrometric evidence (I.R. and U.V.) to be free from benzene.

In the case of camphor, the borneol-isoborneol mixture obtained by reduction was isolated by removing the ethanol under reduced pressure. The residue was then dissolved in benzene, the solution was filtered free of any inorganic material, and the mixture of epimers was recovered by removal of the benzene under reduced pressure.

The compositions of the mixtures of isomers of ± 2-, ± 3- and 4- methylcyclohexanols were determined from their densities using the values for the cis and trans derivatives given by Macbeth et al. (31). The compositions of (+) borneol- (-) isoborneol mixtures were determined from the optical rotation of the mixtures. Estimation of the epimeric mixtures of ± 2:2:6- trimethylcyclohexanols and of ± 2-methylcyclopentanols was effected from the melting points of the 3:5-di-

nitrobenzoates of the mixtures. Attempts to separate ± 3-methylcyclopentanols were unsuccessful. Attempts to estimate the proportion of epimers in mixtures of ± 2-methylcyclopentanols and of ± 2-methylcyclohexanols by means of vapour phase chromatographic analysis (32), were unsuccessful.

± 2:2:6-Trimethylcyclohexanols.

Separation of the epimeric ± 2:2:6-trimethylcyclohexanols was effected by chromatography; final purification was achieved via their 3:5-dinitrobenzoates. The melting points of the epimers and of their 3:5-dinitrobenzoates are given in Table 1.

Table 1

m.p.s. of cis-and trans- (±) 2:2:6-trimethyl cyclohexanols and their 3:5 dinitrobenzoates

	(±)2:2:6-trimethyl cyclohexanol	3:5-dinitrobenzoate
cis	62-63°	124°
trans	48-49.5°	135°

The lower melting epimer was assigned the trans configuration i.e. with the hydroxyl at C_1, and the methyl groups at C_2 and C_6 equatorial, since it was obtained by reduction of (±) -2:2:6-trimethylcyclohexanone with sodium and moist ether (Masson (33)). Moreover the higher melting

epimer was eluted first in the chromatographic separation indicating that it is sterically more hindered and therefore the cis isomer, (cf. Vavon's separation of borneol-isoborneol mixtures by chromatography (34)).

The composition of the mixture of ± 2:2:6-trimethylcyclohexanols obtained by hydrogenation of the ketone was determined by preparing the 3:5-dinitrobenzoate of the mixture and comparing its melting point with the melting points of a standard series of mixtures, (experimental p. 35).

± 2-methylcyclopentanols.

The reduction of ± 2-methylcyclopentanone with sodium and moist ether gave predominantly trans- ± -2-methylcyclopentanol from which the 3:5- dinitrobenzoate m. 87-88° corresponding to the trans ester obtained by Huckel (27), and by Umland and Jefraim (28), was prepared. Catalytic reduction of ± 2- methylcyclopentanone in ethanol over Raney Nickel catalyst gave a mixture of epimers whose 3:5- dinitrobenzoate melted at 72.5°. After successive recrystallisations from ethanol the melting point was raised to 119-120°. The cis- 3:5- dinitrobenzoate therefore corresponds to the isomer obtained by Huckel and Kindler (25), by hydrogenation over platinum catalyst. It would appear that the cis- isomer (m. 86°) claimed by Umland and Jefraim (loc. cit.) was a mixture of cis- and trans- esters. Indeed it was found that a

mixture of cis- and trans- esters containing 78% of the cis- ester melted at 86° and it was difficult to recover the pure cis- ester from such a mixture by fractional crystallisation. Umland and Williams (52), obtained a small quantity of 3:5-dinitrobenzoate m.101-4°, from the product of catalytic hydrogenation of 2-methylcyclopentanone over Adams' platinum catalyst in acetic acid.

± 3-Methylcyclopentanols.

The mixture of epimers obtained by hydrogenation of ± 3-methylcyclopentanone yielded a dinitrobenzoate which melted at 94.5-96°. When other methods of reduction were used, the product yielded a dinitrobenzoate of similar melting point in every case, (table 2). Recrystallisation gave an ester of melting point 108.6°.

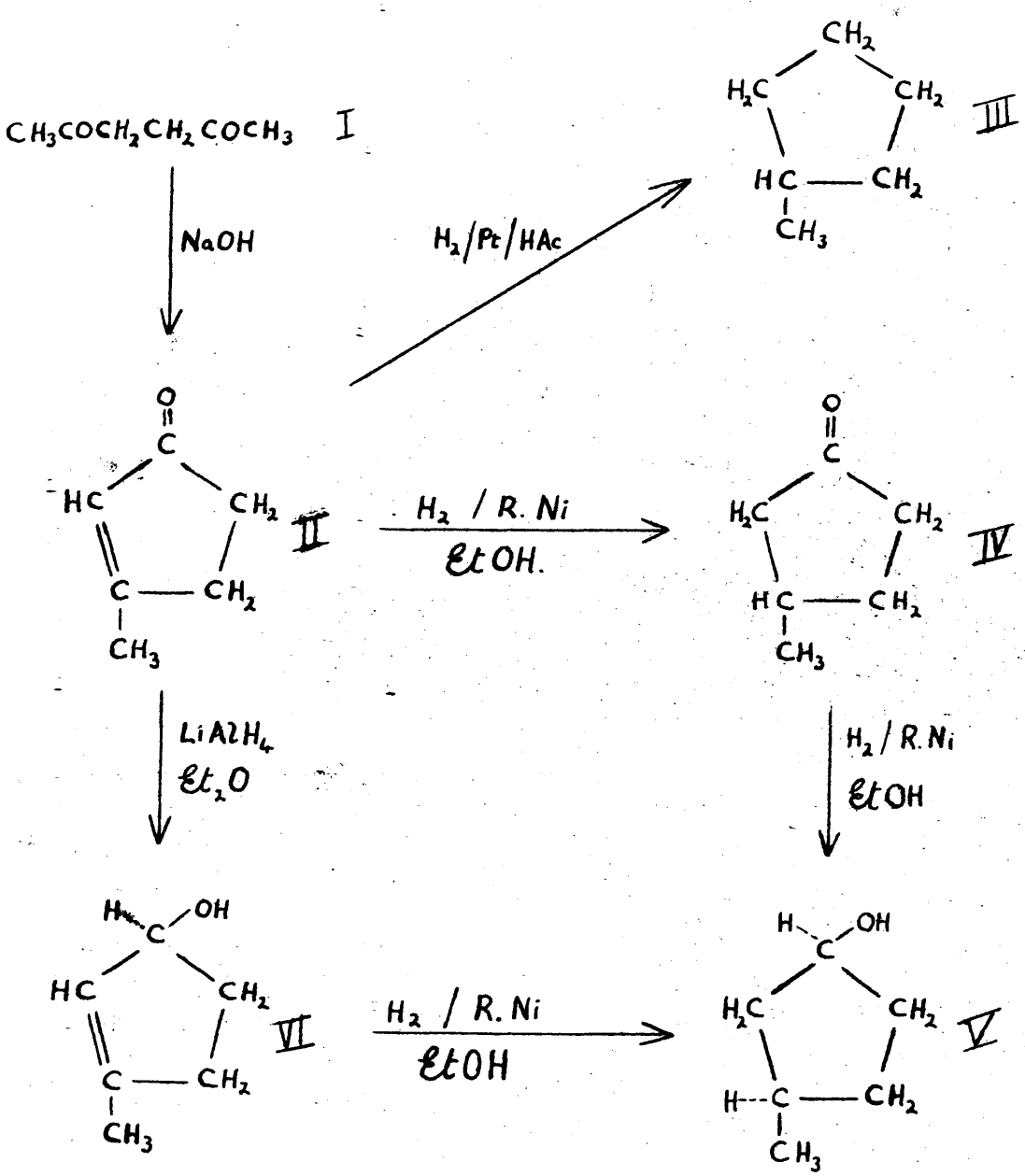
Table 2
Reduction of ± 3-Methylcyclopentanone

Reduction method.	Percentage recovery of ± 3-methylcyclopentanols.	m.p. of 3:5-dinitrobenzoate
Pt/HA/HBr	40	90-93°)m.107.6-108.6 after successive recrystallisations from ethanol
Raney Nickel	88	94.5-96°
$Na/Et_2O/H_2O$	80	94.5-96°
$Al(OPr)_3$	82	92.5-95.5
$LiAlH_4$	62	94.5-96°

It would appear that the same epimer was formed predominantly by every reduction method and since it was obtained

FIGURE 1.

FIGURE 1. REDUCTION OF 3-METHYLCYCLOPENT-2-EN-1-ONE.



by reduction with sodium, it was assumed to be the trans-isomer. The p- nitrobenzoate melted at 71-72.5°.

In an attempt to prepare the cis-isomer, the reduction of 3-methylcyclopent-2-en-1-one (figure I, II) was studied. 3-Methylcyclopent-2-en-1-one was prepared by intramolecular condensation of acetonylacetone (35). Hydrogenation over Adams' platinum oxide catalyst gave methylcyclopentane (III); hydrogenation over Raney Nickel in ethanol gave 3-methyl-cyclopentanol (V) via the saturated ketone (IV); reduction with lithium aluminium hydride under mild conditions (29), yielded 3-methylcyclopent-2-en-1-ol (VI) which readily eliminated water and polymerised under acid conditions. 3-methyl-cyclopent-2-en-1-ol was hydrogenated over Raney Nickel and a 3-methylcyclopentanol (V) was isolated. In both cases the 3-methylcyclopentanol obtained gave the 3:5-dinitrobenzoate m. 108° after recrystallisation from ethanol. Since the cyclopentene ring is planar, catalytic reduction in which cis addition to the double bond occurs (36), would be expected to produce cis-3-methylcyclopentanol preferentially from 3-methylcyclopent-2-en-1-ol. Since reduction of 3-methyl-cyclopentanone with sodium and moist ether yielded preponderantly the same isomer, it would seem that cis-3-methycyclopentanol is more stable than the trans isomer (cf. 1:3-disubstituted cyclohexanes).

It has been shown that the cyclopentane ring is puckered (37), and that compounds such as α-halocyclopentanones exist in preferred conformations (38). It may therefore be that cis- 1:3- disubstituted cyclopentanes exist in a conformation which is more stable than that of the trans isomers. Some evidence for this is given by the fact that 1:3- dimethylcyclopentanes have been prepared unambiguously (39), and the cis isomer was found to have the lower density and refractive index which would indicate that it has the greater conformational stability (see p. 5).

Since the melting point of the 3:5- dinitrobenzoate of the reduction product of ± 3-methylcyclopentanone was raised from 96 to 108°, the trans-epimer was assumed to be present in minor amount. Separation of the epimers was attempted by chromatography, using alumina as adsorbent, without success. Chromatographic separations of the p-nitrobenzoates and of the 3:5- dinitrobenzoates were unsuccessful also. It was concluded that reduction of ± 3-methylcyclopentanone yielded a mixture of epimeric alcohols in which the trans isomer could not be present to an extent of more than 20-30%. The pure cis-isomer was obtained by hydrolysis of the 3:5-dinitrobenzoate. It had the following physical constants: b_{18} 63.8-64.0, d_4^{25} 0.9094, n_D^{25} 1.4440. Equilibration of the isomer over sodium again gave the mixture from which the

3:5-dinitrobenzoate m. 96° was obtained.

An attempt was made to prepare the trans isomer from the cis isomer by acetolysis of the p- toluenesulphonate under neutral conditions. The product after saponification and conversion to the 3:5- dinitrobenzoate was found to consist of a mixture of isomers from which only the cis epimer was isolated.

The physical constants quoted by Godchot (30), for his epimeric ± 3- methylcyclopentanols were:-

	d_4^{28}	n_D^{28}	m.p. of phenylurethane
cis	0.9092	1.4437	80°
trans	0.9102	1.4446	78°

He found that the rate of saponification of the cis-p-nitro-benzoate was slightly less than that of the trans ester and that the Raman spectra of ± cis-3-methylcyclopentanol in the region between 200 and 800 cm^{-1} was slightly different from that of the trans isomer (40). It may therefore be that his isomers were one and the same.

Effect of Promotion of Raney Nickel Catalyst on the Ratio of Stereoisomers formed by Reduction of Cyclopentanones and Cyclohexanones.

The percentage of thermodynamically less stable isomer in the mixture of epimeric alcohols obtained by reduction

of the corresponding ketone over Raney Nickel and over promoted Raney Nickel is given in table 3. In every case the thermodynamically less stable isomer is the cis isomer with the exception of ± 3- methylcyclohexanol when it is the trans isomer and of ± 3- methylcyclopentanol when it is assumed to be the trans isomer.

Table 3

Percentage of thermodynamically less stable isomer obtained in catalytic reduction of cyclic ketones.

Product	% of less stable isomer			Method of estimation
	Raney Nickel	Platinised Raney Ni + NaOH	Raney Ni + $Et_3N+H_2PtCl_6$ + NaOH	
± 2-methylcyclopentanol	57	63	63	dinitrobenzoate m.p.
± 3-methylcyclopentanol	<30	<30	< 30	-
± 2-methylcyclohexanol	54	62	66	density
± 3-methylcyclohexanol	54	60	65	density
4-methylcyclohexanol	56	-	65	density
± 2:2:6-trimethylcyclohexanol	50	45	45	dinitrobenzoate m.p.
(-) isoborneol	92	95	98	optical rotation

With ± 2-methylcyclopentanol and the cyclohexanols a preponderance of the thermodynamically less stable isomer was obtained; the preponderance was increased slightly but not

significantly by use of promoted catalysts. With 3-methylcyclopentanol the more stable isomer predominated, and the ratio of the isomers did not appear to be affected by the use of promoted catalysts.

Comparison of the reduction of methylcyclopentanones by catalytic and chemical methods.

A comparison of various methods of reduction of methylcyclohexanones was made by Noyce and Denney (12), which indicated that the amount of axial isomer produced was related to steric effects of the reducing agent. The results were summed up by Barton's generalisations (20). The comparison has now been extended to methylcyclopentanones (table 4).

The results indicate that reduction with sodium and moist ether gave preponderant formation of the more stable isomer. Indeed cis± 3- methylcyclopentanol was formed predominantly by all the methods investigated. The reduction of ± 2-methylcyclopentanone by lithium aluminium hydride and by aluminium isopropoxide led to an increased amount of the thermodynamically less stable cis isomer; catalytic hydrogenation gave a preponderance of the cis isomer. The reduction of ± 2-methylcyclopentanone was therefore found to conform with Barton's generalisations whereas 3-methylcyclopentanone did not conform re catalytic reduction in acid medium. Huckel (27), claimed that reduction of ± 2-methylcyclopentanone with

Table 4

Reduction of cyclopentanones by catalytic and chemical methods.

Method of Reduction	Product		
	± 2-methylcyclopentanol % cis		± 3-methylcyclopentanol % trans
$Na/Et_2O/H_2O$	8	10*	20-30
$LiAlH_4$	25	25	"
$NaBH_4$	-	26	-
$Al(OPr)_3$	40	76	20-30
Catalytic hydrogenation (Pt/neutral solution	-	28	-
(Pt/HAc/HBr	60	-	20-30
(Raney Ni	57	-	"
(Promoted Raney Ni	63	-	"

* Umland and Williams (52)

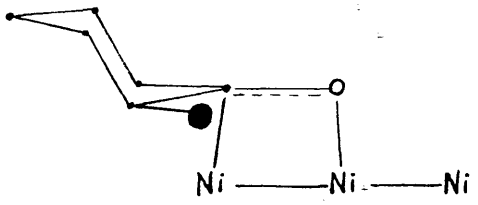
aluminum isopropoxide yielded 70% of cis isomer but his claim was based on a 'pure' cis isomer which must have contained at least 50% of the trans isomer. Since this work was completed, Umland and Williams (52), have published results for the reduction of ± 2-methylcyclopentanone. The analysis of mixtures of isomers obtained by them, was by the method of Umland and Jefraim (28), based on an incompletely separated cis-3:5-dinitrobenzoate (see p. 13). Consequently their results are higher in cis isomer than they should be. Their results are included in table 4 for comparison.

Mechanism of the Catalytic Hydrogenation of Ketones.

Vavon (6) was the first to attempt to explain the stereochemical course of catalytic reduction of cyclohexanones, suggesting that the main factor involved was steric hindrance of the addition of hydrogen to an intermediate ketone-catalyst complex. Linstead (41), suggested that steric interaction between the substituent groups of the ketone and the catalyst surface was the important factor. Both these workers assumed planarity of the cyclohexane ring.

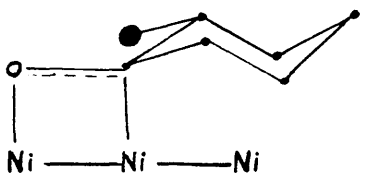
FIGURES 2, 3, 4 & 5.

FIGURE 2.



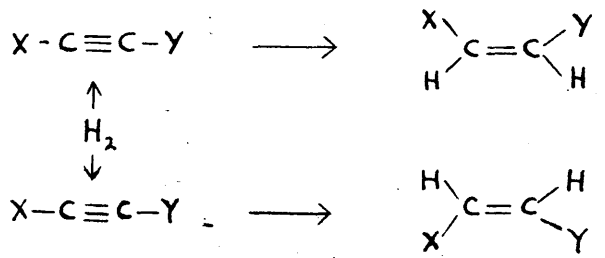
ADSORPTION COMPLEX WHICH YIELDS THE EQUATORIAL-AXIAL ISOMER, UPON ADDITION OF HYDROGEN.

FIGURE 3.



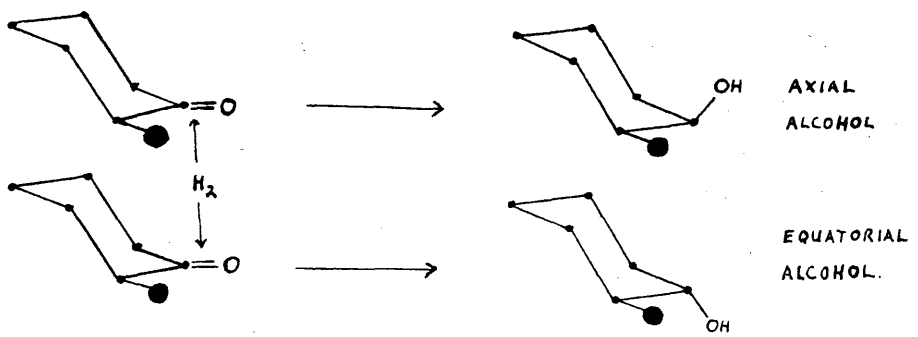
ADSORPTION COMPLEX WHICH YIELDS THE EQUATORIAL-EQUATORIAL ISOMER.

FIGURE 4.



ADDITION OF HYDROGEN TO AN UNSYMMETRICALLY SUBSTITUTED ACETYLENE.

FIGURE 5

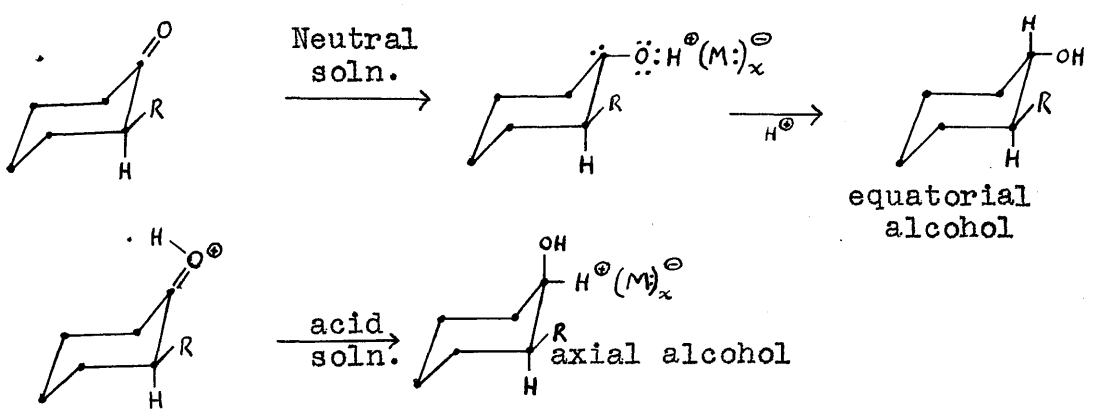


ADDITION OF HYDROGEN TO A SUBSTITUTED CYCLOHEXANONE.

Siegel (42), interpreted the hydrogenation of mono-substituted cyclohexanones in terms of the concept of conformational analysis. He assumed that the cyclohexanone molecule in which the substituent is in the equatorial position and the carbonyl group is included with the adjacent carbon atoms in one plane, is adsorbed without change in the conformation so that the C = O is attached to the catalyst surface at two points C and O. He suggested that the least hindered arrangement is one in which the cycle tilts away from the surface of the catalyst. This is illustrated for 2-methylcyclohexanone in figure 2. Addition of hydrogen from the direction of the catalyst leads to formation of an equatorial C-H bond and consequently to the formation of an axial hydroxyl group. With 2- and 4- substituted cyclohexanones, catalytic hydrogenation therefore yields the cis isomer; with 3-substituted cyclohexanones the trans isomer is obtained. Siegel suggested that the stereo-specificity of the reaction arises from interactions between the substituent and the atoms of the cycle combined with the requirement of a precise orientation of the carbonyl group on the surface of the catalyst.

Brewster (43), pointed out that on the steric grounds suggested by Siegel, this broadside-on mechanism of adsorption of a substituted cyclohexanone on the catalyst surface

would produce the axial alcohol in both neutral and acidic media. Since it had been concluded from a study of the products of hydrogenation of ethylenes, acetylenes and aromatic compounds, that cis addition of hydrogen to a double bond occurs (36,41), the various proportions of isomers produced by hydrogenation of cyclic ketones under different conditions, prompted Brewster to suggest that there is a fundamental difference in the mechanism of such hydrogenation. He therefore proposed the following mechanisms:-



(M = metal catalyst)

in which he suggested that ketones can accept a proton from the solvent and the equivalent of a hydride ion from the catalyst in the distinct steps shown above and that the formation of equatorial or axial alcohol depends on which step occurs first. This mechanism is however subject to the same criticism which he applied to Siegel's - namely the

implication of stereospecificity. The formation of the equatorial alcohol in neutral solution should be stereospecific, yet the results for reduction with Raney Nickel catalyst show that this is not so; indeed with sterically hindered ketones, e.g. camphor, catalytic hydrogenation invariably gives a preponderance of the thermodynamically less stable isomer. Moreover he ignores that there is a fundamental difference between the structure of cyclic ketones and unsaturated hydrocarbons. For example with unsymmetrically substituted acetylenes cis addition to one or other side of the double bond produces the same isomer, (fig. 4, opp. p. 21). With cyclic ketones the configuration of the isomers produced is not related to the substituents about the unsaturated bond but to the substituents of the ring. Different isomers must necessarily be produced by cis addition of hydrogen to one or other side of the molecule, (fig. 5, opp. p. 21). The mechanism of reduction of cyclic ketones may therefore be explained by Siegel's theory with the modification that the cyclohexanone molecule may be adsorbed to give either a ketone catalyst complex formed by equatorial attachment of the carbon atom of the C = O group to the catalyst surface (fig. 2, opp. p. 21) or a complex formed by axial attachment (fig. 3) according to which side of the molecule approaches the catalyst surface. Steric interaction

between the surface and the axial hydrogen atoms at C_3 and C_5 will cause some hindrance to the formation of the complex with an axial carbon to catalyst bond. The complex with an equatorial carbon to catalyst bond will therefore predominate, and addition of hydrogen from the catalyst to this complex will yield the axial alcohol. Brewster's criticism of this mechanism arises from the assumption that the equatorial complex is formed exclusively.

Since Wicker (see p. 6) had shown that the Skita rule does not apply to the reduction of cyclohexanones and that the axial alcohol is not necessarily formed predominantly under acid conditions, he dismissed the Brewster mechanism as irrelevant and returned to Siegel's. He modified it by suggesting that the equatorial alcohol results from the methylcyclohexanone conformation which has an axial alkyl substituent; an axial hydroxyl group is still formed but the product, the axial-axial alcohol passes rapidly into the more stable equatorial-equatorial form. (While this modification accounts satisfactorily for the formation of the more stable isomer from simple cyclohexanones, it does not account for its formation from rigid molecules such as cholestan-3-one which exist in one conformation only.) Wicker also suggested that enol forms contribute in some cases to the formation of the stable equatorial-equatorial

isomer and concluded that prediction of the stereoisomeric composition of the products of catalytic hydrogenation is impossible unless the conformational and tautomeric composition of the ketone is known. At room temperature, however, hydrogenation of ketones has been found to proceed exclusively via the keto- form (44), so that the considerable proportion of more stable isomer obtained in hydrogenations at room temperature cannot be produced from the enol form.

Vavon (6), and Cornubert (9) have shown that the proportion of isomers is related to the catalyst activity, a high proportion of the thermodynamically less stable isomer being produced with a catalyst of high activity. This may be explained in two ways:-

(1) a more active catalyst would give a preponderance of the axial alcohol formed from the preponderant equatorial complex (i.e. the complex formed with an equatorial bond between the carbon atom of the C = O and the catalyst (fig. 2, opposite p. 21), while a less active catalyst would be selective; the energy change for the overall process $>C = O + H_2 \longrightarrow -\overset{|}{\underset{|}{C}}-OH$ is greater in the formation of the more stable isomer which will therefore be formed to a greater extent with a less active and consequently more selective catalyst.

(2) the hydrogenation reaction is reversible:-

$$>C = O + H_2 \rightleftharpoons >CHOH$$

The less stable isomer is formed preferentially owing to the steric interaction of ketone and catalyst but the reversibility of the reaction permits the slow conversion to the thermodynamically more stable isomer. With an inactive catalyst, the increased time for hydrogenation would allow the conversion to proceed further.

In order to test the second possibility, attempts were made to equilibrate the less stable isomer of a cyclic alcohol under the conditions of hydrogenation, by shaking a solution of the substance with a hydrogenation catalyst in a hydrogen atmosphere. Cis- and trans ± 2-methylcyclohexanols and α- and β- cholestan-3-ols were used in these equilibration studies. Cis- ± 2-methylcyclohexanol and α-cholestan-3-ol were obtained by reduction with Adams' platinum catalyst in acid medium of ± 2-methylcyclohexanone and cholestan-3-one respectively. Trans ± 2-methylcyclohexanol was prepared by reduction of ± 2-methylcyclohexanone with sodium and ethanol. β-Cholestan-3-ol was produced by hydrogenation of cholesterol with platinum catalyst in acid medium.

No appreciable amount of equilibration occurred when α- cholestan-3-ol was shaken with Raney Nickel in ethanol for 15 hours at room temperature, nor when it was shaken with

Adams' platinum catalyst in dibutyl ether at 60° for a similar length of time. These experiments were repeated with cis ± 2-methylcyclohexanol; again no appreciable equilibration occurred.

Wicker (22), has recently shown that equilibration of cyclohexanols can be achieved by heating them with alkaline hydrogenation catalysts such as nickel or platinum in an atmosphere of hydrogen, and that equilibration can be brought about at room temperature if sufficient catalyst is used. The following results were abstracted from his paper:-

Compound	Temp.	Cat. %	Reacn. time (hrs.)	Stable isomer % in product
3:3:5-trimethyl-cyclohexanol (89% trans)	140°	Pt 5	5	18 (cis)
	85°	Ni 2.5	66	76 "
	20°	Ni 50	18	72 "

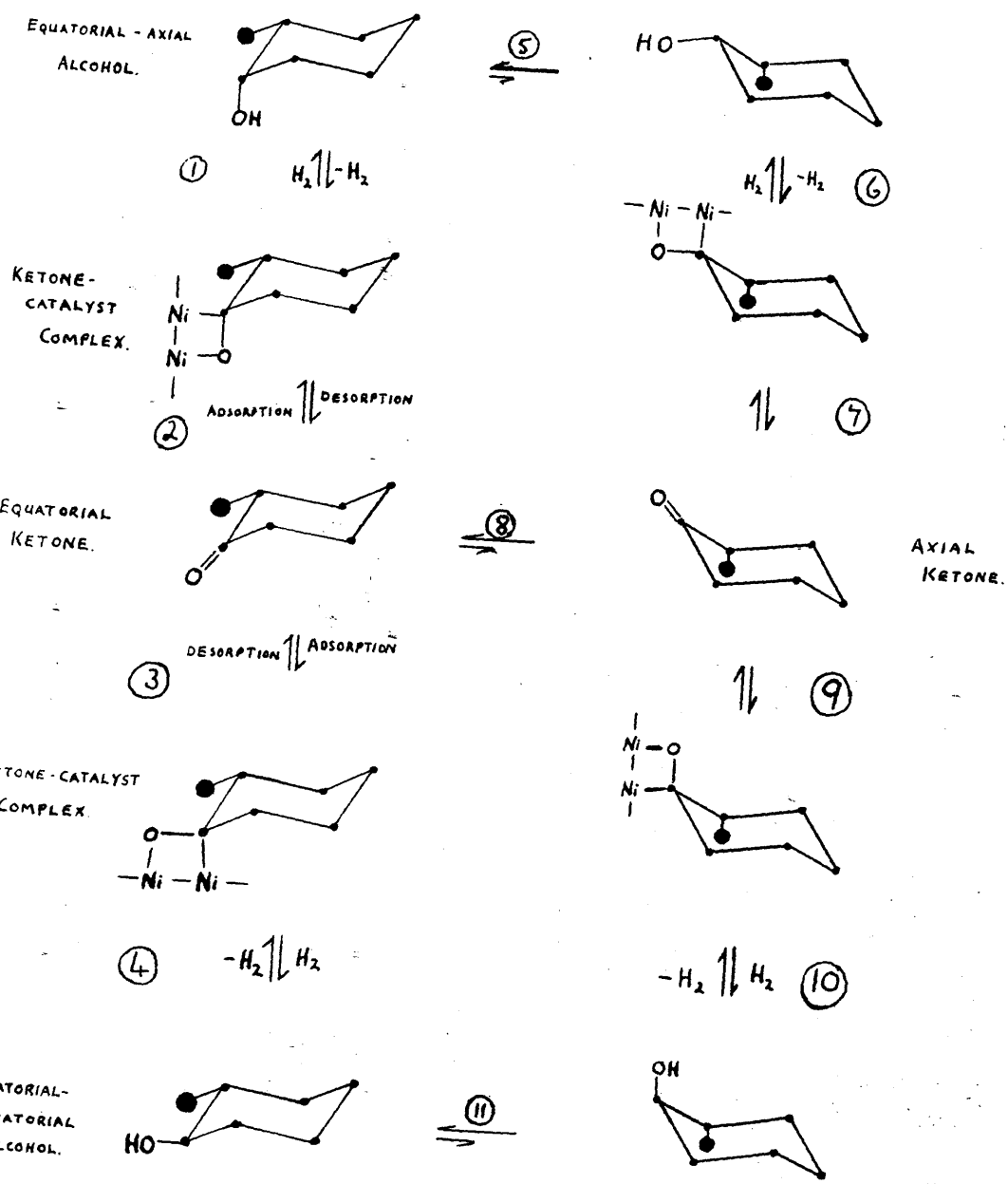
(The equilibrium mixture was found to contain 76% cis isomer.) His result with platinum showed that little equilibration was obtained although he used a much higher temperature (140°), than was used in the present work (60°). His results with nickel catalyst however, are in contradiction with those of the present work. It would seem that this was owing to the

fact that while Wicker obtained equilibration with undiluted cyclohexanol and catalyst, in the present work equilibration was attempted in a considerable excess of ethanol solvent. When cis $\overset{+}{-}$ 2-methyl-cyclohexanol was shaken with Raney Nickel from which ethanol had been decanted, some isomerisation was observed at room temperature. The evidence however, indicates that under the experimental conditions of hydrogenation used in the present work, the proportion of epimeric alcohols is not affected to any great extent by isomerisation. Wicker came to the same conclusion. It would therefore appear that the proportion of isomers is related to the activity of the catalyst and the readiness with which it forms the equatorial ketone-catalyst complex rather than to a thermodynamically controlled reversible reaction.

Equilibration has also been achieved by refluxing an ethanolic solution of a cyclohexanol over Raney Nickel. Such a method obviates the need for an atmosphere of hydrogen. A mixture of α- and β- cholestan-3-ols containing 23% of the α- isomer was obtained from α- cholestan-3-ol. Further reflux with fresh catalyst did not vary this percentage. A similar experiment with β- cholestan-3-ol gave a mixture containing 20% of the α- isomer. Analyses of the mixtures were effected by means of a melting point composition diagram and by chromatographic separation. Equilibration of cis- $\overset{+}{-}$ -2-methylcyclohexanol by the same method gave a mixture

FIGURE 6.

FIGURE 6. EQUILIBRATION OF 2-METHYLCYCLOHEXANOL.



containing 15% of the cis isomer. It may be inferred that dehydrogenation of the cyclohexanol is occurring over Raney Nickel in refluxing ethanol to form the ketone which is re-hydrogenated at the expense of ethanol, thus dispensing with the need for an atmosphere of hydrogen in which to conduct the equilibration. (Mozingo (45), has reduced ketones in ethanol by refluxing the solution over Raney Nickel.) A complex equilibration may be visualised involving the two conformations of the ketone, their adsorption complexes with the catalyst and the conformations of the isomeric cyclohexanols. This is illustrated for 2-methylcyclohexanol in figure 6.

To account for the isomerisation of cyclohexanols, Wicker (loc. cit.), suggested the following mechanism:-

trans alcohol $\rightleftharpoons$ ketone (e-alkyl) $\rightleftharpoons$ ketone (a-alkyl) $\rightleftharpoons$ cis alcohol.

Since, however, he has already suggested (see p. 24), that in the hydrogenation of substituted cyclohexanones, the equatorial alcohol results from the axial ketone, it might have been more logical to postulate:-

cis alcohol $\rightleftharpoons$ ketone (e-alkyl) $\rightleftharpoons$ ketone (a-alkyl) $\rightleftharpoons$ trans alcohol

which is essentially steps $1 \longrightarrow 2 \longrightarrow 8 \longrightarrow 9 \longrightarrow 10$ (fig. 6). Such a mechanism does not account for isomerisation of rigid molecules such as cholestan-3-ol. It would therefore appear

that while for simple cyclohexanols some equilibration occurs by Wicker's mechanism, the important steps in the isomerisation are steps 1 ⟶ 2 ⟶ 3 ⟶ 4, in which the axial alcohol is dehydrogenated to the ketone; when the ketone is readsorbed by the catalyst, some catalyst-ketone complex is formed by axial attachment of the carbon atom of the carbonyl group and leads to formation of the equatorial alcohol (see p. 23). In a quantitative study of conformational analysis, Winstein and Holness (46), have estimated that the amount of cis-2-alkylcyclohexyl ester which exists in the equatorial-ester axial-substituent conformation is about 20%. It is therefore to be expected that with simple alkyl-cyclohexanols some of the axial equatorial isomer exists in the conformation with the hydroxyl group equatorial and that some equilibration also occurs by steps 6 ⟶ 7 ⟶ 9 ⟶ 10.

EXPERIMENTAL

Hydrogenation of cyclic ketones. The hydrogenation of cyclic ketones over Raney Nickel and promoted Raney Nickel catalysts is described in part 1, pp. 23-54.

Recovery of the alcohol product of hydrogenation. The recovery of the product of hydrogenation is detailed in part 1, p. 57.

Determination of percentage of cis isomer. The percentage of cis isomer present in a mixture of cis and trans methylcyclohexanols was determined from the density of the mixture and the densities of the pure isomers given by Macbeth et al. (31). The percentage of axial isomer (α), is given by the relation $\alpha = \frac{d-d_1}{d_2-d_1}$, where d is the density of the mixture of isomers and d_1 and d_2 are the densities of the equatorial and axial isomers respectively. The density of the mixture of isomers was determined in a pyknometer of 5 ml. capacity using a thermostat bath which was regulated to $30 \pm 0.02^{\circ}$ C. The results are given in table 5.

TABLE 5. The percentage ($\varkappa$) of axial isomer obtained by hydrogenation of methylcyclohexanones.

Catalyst system	Cyclohexanol product	d	d_1	d_2	$\varkappa$
Raney Nickel	2-methyl	0.9228	0.9174	0.9274	54
Platinised Raney Nickel + NaOH	"	0.9236	"	"	62
Raney Nickel + Et_3N + H_2PtCl_6 + NaOH.	"	0.9240	"	"	66
Raney Nickel	3-methyl	0.9107	0.9072	0.9137	54
Platinised Raney Nickel + NaOH	"	0.9111	"	"	60
Raney Nickel + Et_3N + H_2PtCl_6 + NaOH	"	0.9114	"	"	65
Raney Nickel	4-methyl	0.9115	0.9040	0.9173	56
Raney Nickel + Et_3N + H_2PtCl_6 + NaOH	"	0.9127	"	"	65

The percentage of (-)isoborneol in the hydrogenation of (+) camphor was obtained from the optical rotation of the (+) borneol (-) isoborneol mixture. The percentage of (-) isoborneol $\varkappa = \frac{\alpha - \alpha_1}{\alpha_2 - \alpha_1}$ where α, α_1, and α_2 are the rotations of ethanolic solutions of the isomeric mixture, (+) borneol, and (-) isoborneol respectively. α was determined for a 10% solution in ethanol. The results are given in Table 6.

TABLE 6. Percentage (x) of (-) isoborneol obtained in the product of hydrogenation of (+) camphor.

Catalyst system	α	α_1	α_2	x
Raney Nickel	-28.9	+37.4	-34.2	93
Platinised Raney Nickel + NaOH	-32.3	"	"	97
Raney Nickel + Et_3N + H_2PtCl_6 + NaOH	-32.9	"	"	98

Separation and Identification of cis- and trans (±) -2:2:6- trimethyl-cyclohexanols. The cis and trans isomers of (±) -2:2:6- trimethyl-cyclohexanol were separated by the chromatographic method used by Vavon and Gastambibe for borneol-isoborneol mixtures (34). 2:2:6- Trimethylcyclo-hexanol (12.0g.) was dissolved in petroleum ether (100 ml, 40-60) and the solution was passed through a chromatogram tube containing a column of alumina (30 x 4 cm). The column was eluted with various solvents and fractions were collected as detailed in Table 7.

Table 7

Separation of cis- and trans-(±)-2:2:6- trimethylcyclohexanols

Fraction	Eluant		Alc. eluted amt. in g.	% cis.	3:5 dinitrobenzoate m.p.
1	Pet. ether	400 ml	0.43	97	118-123
2	" "	400 ml	0.51	66	100-107
3	" "	800 ml	0.42	60	98-102
4	" "	1,500 ml	0.39	60	98-102
5	C_6H_6	500 ml	0.27	50	98-104
6	"	1,300 ml	1.31	50	98-104
7	"	1,800 ml	0.42	45	101-106
8	EtOH	300 ml	5.15	12	122-130
9	"	300 ml	0.20	-	-
10	"	300 ml	-	-	-

Total alcohol recovered 9.50 g.

The 3:5 dinitrobenzoates of fractions 1 and 8 were prepared and recrystallised from ethanol until of constant melting point.

Fraction 1 - 3:5 dinitrobenzoate m.124° (C,H,N (found) 57.30, 6.29, 8.34. (calc.) 57.12, 6.00, 8.34)

Hydrolysis of the ester gave an alcohol m.62-63°.

Fraction 8 - 3:5 dinitrobenzoate m.135° (C,H,N (found) 57.25, 5.77, 8.52)

Hydrolysis of the ester gave an alcohol m.48-49.5°.

A series of mixtures of the two dinitrobenzoates was made up and their melting points were determined (table 8).

Table 8

Mixed melting points of cis- and trans- (±)-2:2:6-trimethylcyclohexyl-3:5-dinitrobenzoates

% cis	melting point	% cis	melting point
1	130-135	50	102-104
9	122-131	60	100.5-102.5
17	117-128	70	100.5-111
25	103-124	80	102-115.5
31	103-118.5	90	111.5-120.5
35	102-114	95	118 -122.5
40	102-110	99	122 -124

From the melting points of the 3:5 dinitrobenzoates of the products and their mixed melting points with the pure esters, the percentages of cis isomer in the products obtained from the hydrogenation of (±)-2:2:6-trimethylcyclohexanone over Raney Nickel and promoted Raney Nickel catalysts were found, using a diagram compiled from table 8. The results are given in table 9.

Table 9

Percentage of cis-(±)-2:2:6-trimethylcyclohexanol in the product of hydrogenation of (±)-2:2:6-trimethylcyclohexanone.

Catalyst system	Product			
	% rec.	b.p.	3:5 dinitrobenzoate m.p.	% cis
Raney Nickel	92	b_{18} 81-82°	100-104	50
Platinised Raney Nickel + NaOH	91	b_{18} 82-84°	100-106	45
Raney Nickel + Et_3N + H_2PtCl_6 + NaOH	90	b_{18} 82-84°	100-106	45

Preparation of methylcyclopentanones. Part I, p. 38.

Hydrogenation of methylcyclopentanones over Raney Nickel and promoted Raney Nickel catalysts. Part I, p. 25.

Reduction of methylcyclopentanones with sodium and moist ether (48). Sodium wire (3.95 g.) was added in pieces to a solution of methylcyclopentanone (4.90 g.) in diethyl ether (40 ml.) and water (7.5 ml.). The reaction mixture was stirred and cooled in a water bath to moderate the reaction. When the sodium had dissolved, the two layers which had formed were separated; the ether layer was washed with dilute hydrochloric acid (5 ml., 6 N), then with water (5 ml.) and dried over $MgSO_4$ (10 g.). The ether was stripped off and the residue was distilled under reduced pressure.

(±) 2-methylcyclopentanol, yield 85%, b_{18} 58-62°,
3:5-dinitrobenzoate m.80-83°.

(±) 3-methylcyclopentanol, yield 82%, b_{36} 75-76°,
3:5-dinitrobenzoate m.94.5-96°.

Reduction of (±)-2-methylcyclopentanone with sodium and alcohol yielded (±)-2-methylcyclopentanol in only 30% yield and a considerable amount of high boiling residue.

Reduction of methylcyclopentanones with lithium aluminium hydride (12). Methylcyclopentanone (4.90 g.) in anhydrous diethyl ether (50 ml.) was added with stirring to a flask containing lithium aluminium hydride (3.80 g.) and ether 120 ml.) at such a rate as to maintain gentle reflux. Refluxing was continued for 6 hours after the addition had been completed. The flask was cooled; ice-cold water was added drop by drop with constant stirring and cooling until excess lithium aluminium hydride had reacted. The resulting white suspension was added to ice water (50 ml.), dilute sulphuric acid was added, and the mixture was stirred to dissolve the suspension. The ether layer was separated off; the aqueous layer was extracted with more ether (2 x 50 ml.) and the combined ether extracts were dried over $MgSO_4$. The reduction product was then recovered by distillation.

(±)-2-methylcyclopentanol, yield 67%, b_{21} 62-64°,
3:5-dinitrobenzoate m. 72-74°.

(±)-3-methylcyclopentanol, yield 62%, b_{18} 61-63°,
3:5-dinitrobenzoate m.94.5-96.0°

Reduction of methylcyclopentanones with aluminium isopropoxide (50). Methylcyclopentanone (9.80 g., 0.1 mole.) in isopropyl alcohol (120 ml.) was added to aluminium isopropoxide (20 g.) in isopropyl alcohol (70 ml.) contained in a 500 ml. flask equipped with fractionating column, stillhead, condenser and receiver. The flask was refluxed gently to maintain a temperature of 60-70° at the still-head until the dinitrophenylhydrazine test for acetone in the distillate was negative. The isopropyl alcohol was removed under reduced pressure (120 mm.). Dilute sulphuric acid (1:6, 120 ml.) was added; the oily layer was separated off; the acid layer was extracted with benzene (2 x 50 ml.), and the combined extracts were dried over magnesium sulphate. The benzene and isopropyl alcohol were distilled off through a bead-packed column, which was then washed down with ether. The ether was distilled off and the reduction product obtained by distillation.

(±)-2-methylcyclopentanol b_{12} 54-58°, yield 80%,
3:5-dinitrobenzoate m.64-65°.

(±)-3-methylcyclopentanol b_{30} 71-73°, yield 82%,

3:5 dinitrobenzoate m.92.5-95.5°.

Reduction of methylcyclopentanones with Adams' Platinum Catalyst, (8). Methylcyclopentanone (4.90 g.) in acetic acid (100 ml.) containing a small amount of hydrobromic acid (1 ml.) was hydrogenated over platinum oxide catalyst (1.0 g., supplied by Johnson-Matthey Co. Ltd.). The rate of hydrogenation was slow, only half the theoretical amount of hydrogen being absorbed. After hydrogenation, the acid solution was treated with sodium hydroxide (2 g. NaOH in 4 ml. H_2O) and filtered. Acetic acid was removed from the filtrate under reduced pressure. The residue was saponified with alcoholic potassium hydroxide; the hydroxide solution was neutralised with dilute hydrochloric acid and was extracted with benzene. The benzene extract was washed with dilute sodium bicarbonate solution and then dried over magnesium sulphate. The hydrogenation product was recovered from the benzene solution by distillation. The results are summarised in Table 10.

Table 10

Hydrogenation of methylcyclopentanones over Adams platinum catalyst

Cyclopentanone	Time for hydrogenation (hrs.)	Vol. of hydrogen absorbed (theor=1200ml)	Product-cyclopentanol	Yield %	3:5-dinitrobenzoate m.p.
2-methyl	24	650	2-methyl	44	73-74.5°
3-methyl	20	650	3-methyl	40	90-93°

Determination of cis:trans ratio of (±)-2-methylcyclopentanols. Trans (±)-2-methylcyclopentyl-3:5-dinitrobenzoate m.87-88° was obtained by recrystallisation of the dinitrobenzoate of the product of reduction of (±)-2-methylcyclopentanone with sodium and moist ether. Cis-(±)-2-methylcyclopentyl-3:5-dinitrobenzoate m.119-120°, (C 55.1, H 4.7, N 9.1; calc. C 54.9, H 4.6, N 9.1), was obtained from the product of hydrogenation of (±)-2-methyl-cyclopentanone over Raney Nickel. Melting points of a series of mixtures were determined (Table 11). From the table a binary melting point diagram was drawn and was used for the estimation of the percentage of cis isomer present in the product from (±)-2-methylcyclopentanone reduced by chemical and catalytic methods.

Table 11

Binary melting points of cis- and trans-(±)-2-methylcyclopentyl-3:5-dinitrobenzoates

% cis dinitrobenzoate	m.p., °C.	% cis dinitrobenzoate	m.p., °C.
10.5	81-82	51.5	68-69.6
21.0	74-76	65.0	73.8-77.2
31.0	69-70.4	78.5	86.0-86.8
42.0	65-66.4	91.0	99.6-102.0

(±)3-Methylcyclopentanols. Recrystallisation of the

3:5-dinitrobenzoate of (±)-3-methylcyclopentanol produced by chemical and by catalytic reduction of (±)-3-methylcyclopentanone yielded in every case the cis-ester m.107.6-108.6°, (C 55.0, H 4.6, N 9.0; calc. C 54.9, H 4.6, N 9.1). From the rise in melting point of the ester, it was estimated roughly that the trans isomer was present to an extent of 20-30% in the reduction product. Saponification of the purified 3:5-dinitrobenzoate with alcoholic potassium hydroxide gave cis-(±)-2-methylcyclopentanol, b_{18} 63.8-64.0°, d_4^{25} 0.9094, N_D^{25} 1.4440, p-nitrobenzoate m.71-72.5°.

Equilibration of cis (±)-3-methylcyclopentanol (49). Cis-(±)-3-methylcyclopentanol (1.0 ml.) was heated for 24 hours with (±)-3-methylcyclopentanone (0.05 ml.) and sodium (0.02 g.) at 120° under nitrogen. After cooling benzene (20 ml.) was added, followed by dilute HCl (4 ml., 6N). The layers were separated; the benzene layer was washed with water and dried over $MgSO_4$. The 3:5-dinitrobenzoate was prepared from the benzene solution, m. 94.5-96°, mixed melting point with the cis-ester m. 101-103°, indicating that equilibration gave a mixture of isomers of similar composition to that obtained by reduction of (±)-3-methylcyclopentanone.

Attempted separation of (±)-3-methylcyclopentanols by chromatography. The separation of (±)-3-methylcyclopentanols obtained by catalytic hydrogenation of (±)-3-methylcyclopent-

anone over Raney Nickel catalyst was attempted by chromatographic adsorption on neutral alumina using petroleum ether (40-60) as solvent and benzene and benzene containing 1% ethanol as successive eluants. The attempts were unsuccessful. Similar attempts with the p-nitrobenzoate and with the 3:5-dinitrobenzoate using petroleum ether (60-80) as solvent and petroleum ether (60-80) containing 1% ethanol as eluant were unsuccessful.

Solvolysis of cis (±)-3-methylcyclopentyl-p-toluenesulphonate (28). ± 3-Methylcyclopentanol (16.0 g.) in dry pyridine (160 ml.) was cooled to -5°. p-Toluenesulphonyl chloride (30.6 g., 1.1 equivs.) was added in one portion and the flask was stoppered. The suspension was swirled until the chloride had dissolved. The reaction mixture was maintained at 0° for 2 hrs., then water was added in portions (1 + 2 + 4 + 8 ml.) at intervals of 5 mins. with swirling and cooling, the temperature not being allowed to rise above 5°. The solution was diluted with water (160 ml.) and was then extracted with chloroform (3 x 200 ml.). The chloroform extract was washed successively with ice cold dilute sulphuric acid, water and sodium bicarbonate solution. The chloroform extract was then dried over $MgSO_4$; it was filtered and evaporated to dryness under reduced pressure. The product was recrystallised from petroleum ether. Yield 21.0 g., m. c.12°.

The p-toluenesulphonate was acetolysed by stirring it with freshly fused potassium acetate (8.45 g.), acid free acetic anhydride (95 ml.) and toluene (100 ml.) for 48 hrs. at 90-100°. The toluene solution was cooled and neutralised with sodium bicarbonate. It was dried and distilled to give the acetate b_{40} 84°, 6.8 g. The acetate was saponified with alcoholic potassium hydroxide and the product was steam distilled from the alkaline solution. The steam distillate was saturated with potassium carbonate and extracted with benzene. The benzene extract was dried($MgSO_4$) and distilled through a bead-packed column to remove benzene and ethanol. The residue was distilled giving (±)-3-methylcyclopentanol (4.10 g.) b_{18} 64.0-64.5°. The 3:5-dinitrobenzoate was prepared - m.98.5-99.6°, mixed melting point with cis-(±)-3-methylcyclopentyl-3:5-dinitrobenzoate 103-104°, indicating that the mixture obtained consisted chiefly of the cis-isomer.

Preparation of 3-methylcyclopent-2-en-1-one (35). Acetonylacetone (102.5 g.) was added rapidly to a boiling solution of sodium hydroxide (8.55 g.) in water (855 ml.). After refluxing for 15 mins., the dark brown solution was quickly cooled to room temperature, saturated with sodium chloride and extracted three times with ether (500, 250 and 250 ml.). The extracts were washed with water (3 x 15 ml.), dried and

evaporated down to remove the ether. On distillation the residual dark brown ketone oil gave the ketone (48.5 g., 57%), 2:4-dinitrophenylhydrazone m. 183-5°, oxime m. 140° (N = 12.4%, calc. 12.6%).

Hydrogenation of 3-methylcyclopent-2-en-1-one.

(a) 3-Methylcyclopent-2-en-1-one (15.0 g.) in acetic acid (60 ml.) was hydrogenated over platinum oxide catalyst (1.0 g.). Approximately 3 moles. of hydrogen were absorbed. Methylcyclopentane (n_D^{18} 1.4096) was recovered.

(b) 3-Methylcyclopent-2-en-1-one (16.0 g.) was hydrogenated over Raney Nickel (3.0 g.) in ethanol (60 ml.). 2 moles. of hydrogen were taken up. 3-Methylcyclopentanol (14.2 g.) was obtained; 3:5-dinitrobenzoate m. 95.5-96°, mixed melting point with cis-(±)-3-methylcyclopentyl-3:5-dinitrobenzoate m. 101-103°.

(c) 3-Methylcyclopent-2-en-1-one (3.0 g.) was hydrogenated over Raney Nickel catalyst (1 g.) in ethanol (40 ml.). Reaction was stopped after 1.0 mole. hydrogen had been taken up. 3-Methylcyclopentanone b_{756} 142-143°, was obtained; yield 1.51 g. Semicarbazone m. 185°.

Reduction of 3-methylcyclopent-2-en-1-one with lithium aluminium hydride. When 3-methylcyclopent-2-en-1-one was reduced with excess lithium aluminium hydride as described for methylcyclopentanones (p. 37), a brittle polymer

(C = 86.9%, H = 10.7%) was obtained. Reduction was therefore conducted under neutral conditions (29). A suspension of lithium aluminium hydride (1.54 g.) in anhydrous ether (100 ml.) was added with stirring to 3-methylcyclopent-2-en-1-one (14.1 g.) in anhydrous ether (100 ml.) at -30° over a period of 15 mins. The reaction mixture was allowed to warm up to 0° and ice was added to decompose the lithium aluminium complex. The ether layer was separated off, washed with water (50 ml.), dried ($MgSO_4$) and the ether was removed under reduced pressure. The residual 3-methylcyclopent-2-en-1-ol was distilled b_{20} 66-67, $n_D^{18.5}$ 1.4753, yield 10.1 g., 80%. An attempt to prepare the 3:5-dinitrobenzoate was unsuccessful. It was found that under acid conditions water was readily eliminated and polymerisation occurred.

Hydrogenation of 3-methylcyclopent-2-en-1-ol. 3-Methylcyclopent-2-en-1-ol (6.5 g.) in ethanol (60 ml.) was hydrogenated over an aged Raney Nickel catalyst (2.0 g.) which was inactive for hydrogenation of the carbonyl group. 1 mole. of hydrogen was absorbed. The product of reduction - 3-methylcyclopentanol (5.06 g.) b_{21} 66-68 - gave a 3:5-dinitrobenzoate m. 96-96.5°. The melting point was not lowered by addition of the dinitrobenzoate prepared from the product of reduction of 3-methylcyclopentanone with sodium and moist ether. Thus the same isomer was produced by reduction of 3-methylcyclo-

pentanone with sodium and moist ether and by hydrogenation of 3-methylcyclopent-2-en-1-ol. This isomer was therefore assigned the cis configuration (see p. 15) and has been designated as such throughout the experimental section.

Preparation of α-cholestan-3-ol (8). Cholestan-3-one (4.0 g.) was hydrogenated over platinum oxide catalyst (1.0 g.) in acetic acid (120 ml.) containing constant boiling hydrobromic acid (1.0 ml.). Time required for hydrogenation - 2 hours. After hydrogenation had been completed, the acid solution was treated with NaOH (2 g.) in water (4 ml.), filtered and evaporated down under reduced pressure. The residue was saponified with alcoholic potassium hydroxide to give the product m. 174-178°. Successive recrystallisations from ethanol gave α-cholestan-3-ol (2.21 g., 55%, m. 184.5-186°).

Preparation of β-cholestan-3-ol. Cholesterol (2.50 g.) was hydrogenated over platinum oxide catalyst (1.0 g.) in acetic acid (75 ml.) at 60°. Time of hydrogenation - 1 hour. The product was saponified with alcoholic potassium hydroxide; recrystallisation from ethanol gave β-cholestan-3-ol (m. 141.5-143, 2.05 g., 82%).

Preparation of (±)-cis-2-methylcyclohexanol. (±)-2-methylcyclohexanone (20 g.) in acetic acid (120 ml.) containing

HBr (1 ml., constant boiling aqueous solution) was hydrogenated over Adams' platinum oxide catalyst (2.0 g.). The product was saponified with alcoholic potassium hydroxide solution. The product was steam distilled from the alkaline solution. The steam distillate was saturated with potassium carbonate and extracted with ether; the ether extract was dried ($MgSO_4$) and distilled. The fraction distilling 60-65 (15 mm.) was esterified with 3:5-dinitrobenzoyl-chloride. The 3:5-dinitrobenzoate was recrystallised from ethanol - m. 102-104°. It was saponified with aqueous potassium hydroxide, steam distilled and the steam distillate was extracted with ether. Cis-(±)-2-methylcyclohexanol (13.0 g., b_{15} 62-63°, d_4^{30} 0.9278) was obtained from the ether extract by distillation.

Preparation of trans-(±)-2-methylcyclohexanol (51).
(±)-2-Methylcyclohexanone (10.0 g.) in aqueous ethanol (20 ml. H_2O:60 ml. EtOH) was reduced by adding sodium wire (14.0 g.) in small pieces. More ethanol was added to prevent the reaction mixture from becoming pasty. When the sodium had dissolved, the solution was steam distilled. The steam distillate was saturated with potassium carbonate and extracted with ether. The ether extract was dried ($MgSO_4$) and distilled. The fraction b_{15} 60-65 was esterified to the 3:5-dinitrobenzoate which after four crystallisations from

ethanol melted at 118.5-120°. Saponification with aqueous potassium hydroxide gave trans-(±)-2-methylcyclohexanol (4.20 g., b 164-166°, d_4^{30} 0.9174).

Equilibration of α-cholestan-3-ol.

(a) α-Cholestan-3-ol (0.5 g.) containing cholestan-3-one (5%; melting point of mixture 176-180.5) was stirred with platinum oxide catalyst (0.5 g., previously reduced at 20° with hydrogen) in dibutyl ether (50 ml.) at 65° for 48 hours under an atmosphere of nitrogen. No equilibration occurred since the mixture was recovered unchanged by filtering off the catalyst and removing the solvent under reduced pressure. 0.47 g. of material (m. 177-180°) was recovered.

(b) α-Cholestan-3-ol (0.5 g.) was stirred with Raney Nickel catalyst (1.0 g.) in ethanol (50 ml.) for 15 hours under an atmosphere of hydrogen. The solution was filtered free of catalyst and evaporated down under reduced pressure to give α-cholestan-3-ol unchanged (0.48 g., m. 181-183°). This experiment was repeated with the addition of 0.2 moles. of NaOH (as a ION solution) to the system; α-cholestan-3-ol (m. 180-182°) was recovered indicating that little equilibration had occurred.

(c) α-Cholestan-3-ol (0.5 g.) was refluxed with Raney Nickel catalyst (1 g.) in ethanol (50 ml.) for 15 hrs. The product (0.45 g.) melted at 146-149°. It was refluxed for

a further 20 hours with fresh catalyst (2 g.) in ethanol (50 ml.) without further change in the melting point. From a binary melting point diagram of α- and β- cholestan-3-ols, the amount of α-cholestan-3-ol in the mixture was estimated to be 25%. The infra-red absorption spectrum of the mixture indicated the absence of ketone. Chromatographic analysis (53), of the mixture (0.40 g.) using alkali free alumina (12 g.) and benzene as solvent and benzene + 1% ethanol as eluant gave 0.082 g. of α-cholestan-3-ol indicating that the mixture contained 20% of the α-isomer.

Equilibration of β-cholestan-3-ol. β-cholestan-3-ol (0.5 g.) was refluxed with Raney Nickel catalyst (2 g.) in ethanol (50 ml.) for 20 hrs. The product after recovery had a melting point 145-7° which was unchanged after repetition of the experiment with fresh catalyst. This corresponded to 22% of α-cholestan-3-ol in the mixture. Chromatographic separation of the mixture indicated that α-cholestan-3-ol was present to the extent of 18%.

Equilibration of cis-(±)-2-methylcyclohexanol. .

(a) Cis-(±)-2-methylcyclohexanol (5.0 g., d_4^{30} 0.9278) was stirred with Raney Nickel catalyst (2 g.) in ethanol (30 ml) under an atmosphere of hydrogen for 7 hrs. The ethanol solution was filtered free of catalyst and the methylcyclohexanol was recovered in the way described previously (p. 57 part I).

Yield 4.15 g., d_4^{30} 0.9274. The result indicated that little equilibration had occurred.

(b) Cis-(±)-2-methylcyclohexanol (5.0 g.) was stirred with Adams' platinum oxide catalyst (1.0 g.) in dibutyl ether (70 ml.) under an atmosphere of hydrogen at 70° for 7 hrs. The cis-isomer was recovered unchanged (4.02 g., d_4^{30} 0.9275).

(c) Cis-(±)-2-methylcyclohexanol (5.0 g.) in ethanol (100 ml.) was refluxed over Raney Nickel (5 g.) for 16 hrs. The methylcyclohexanol was recovered in the usual way (3.70 g., d_4^{30} 0.9190, 15% cis). Further reflux for 16 hrs. with Raney Nickel (3 g.) in ethanol (100 ml.) gave upon recovery of the 2-methylcyclohexanol, 2.36 g. d_4^{30} 0.9189, corresponding to a mixture containing 14% of cis isomer.

(d) Cis-(±)-2-methylcyclohexanol (5.0 g.) was stirred under an atmosphere of hydrogen for 7 hrs. with Raney Nickel catalyst (2.0 g.) from which the ethanol had been decanted. The catalyst was filtered off and washed with ethanol. 2-Methylcyclohexanol was recovered from the filtrate. Yield 3.85 g., d_4^{30} 0.9239, corresponding to a mixture containing 53% of cis isomer.

BIBLIOGRAPHY

(1) Skita, L. Annalen, 1922, 427, 255.
ibid., 1923, 431, 1.

(2) von Auwers, ibid. 1922, 420, 92.

(3) von Auwers and Schmelzer, Chem. Abs., 1928, 22, 4486.

(4) Skita and Faust, Ber., 1931, 64B, 2878.

(5) Vavon, Aziani and Herynk, Bull. soc. chim., 1926, 39, 1138.
Vavon and Callier, ibid., 1927, 41, 357.
Vavon and Anziani, ibid., 1638.
Vavon and Apchié, ibid., 1928, 43, 667.
Vavon and Flurer, ibid., 1929, 45, 764.
Vavon and Nitchovitch, ibid., 961.
Vavon and Guedon, ibid., 1930, 47, 901.

(6) Vavon, ibid., 1931, 49, 937.

(7) Vavon and Jakubowicz, ibid., 1933, 53, 585.

(8) Ruzicka et al., Helv. Chim. Acta, 1934, 17, 1407.

(9) Anziani and Cornubert, Bull. soc. chim., 1945, 12, 359.

(10) Claudon, ibid., 1950, 627.

(11) Jackman, Macbeth and Mills, J.C.S., 1949, 2641.

(12) Noyce and Denney, J.A.C.S., 1950, 72, 5743.
Noyce et al. ibid., 1956, 78, 2579.

(13) Barton and Cookson, Quart. Revs. 1956, X, 44.

(14) Hassel and Viervoll, Acta Chem. Scand., 1947, 1, 149.
Beckett, Pitzer and Spitzer, J.A.C.S., 1947, 69, 2488.

(15) Barton, Hassel, Pitzer and Prelog, Nature, 1953, 72, 1096.

(16) Hassel, Research, 1950, 3, 504.
Quart. Rev., 1953, VII, 221.

(17) Goering and Serres, J.A.C.S., 1952, 74, 5908.
Noyce and Denney, ibid., 5918.
Haggis and Owen, J.C.S., 1953, 408.
Darling, Macbeth and Mills, ibid., 1364.

(18) Allinger, Experientia, 1954, 10, 328.

(19) Kelly, quoted by Barton & Cookson (13).

(20) Barton, J.C.S. 1953, 1029.

(21) Cornubert et al., Bull. soc. chim., 1955, 400.

(22) Wicker, J.C.S., 1956, 2165.
Peppiatt and Wicker, ibid., 1955, 3122.

(23) Vavon and Horeau, Bull. soc. chim., 1934, 1, 1703.
Vavon and Flurer, ibid., 1929, 45, 754.

(24) Godchot and Bedos, Compt. rend., 1926, 182, 393.

(25) Huckel and Kindler, Ber., 1947, 80, 202.

(26) Turner, J.A.C.S., 1950, 72, 878.

(27) Huckel and Sauerland, Ber., 1954, 87, 1003.

(28) Umland and Jefraim, J.A.C.S., 1956, 78, 2788.

(29) Phillips and Mentha, ibid., 142.

(30) Godchot, Cauquil and Calas, Bull soc. chim., 1939, 6,1366.

(31) Macbeth and Mills, J.C.S., 1945, 710.
Jackman, Macbeth and Mills, ibid., 1949, 1719.

(32) Ray, J. Applied Chem., 1954, 4, 21.

(33) Masson, Compt. rend., 1912, 154, 518.

(34) Vavon and Gastambibe, ibid., 1948, 226, 1201.

(35) Acheson and Robinson, J.C.S., 1952, 1127.

(36) A. & L. Farkas, Trans. Far. Soc., 1942, 33, 837.
Waldeland, Zartman and Adkins, J.A.C.S., 1933, 55, 4234.

(37) Kilpatrick, Pitzer and Spitzer, J.A.C.S., 1947, 69, 2483.
Kwart and Vosburgh, ibid., 1954, 76, 5400.
Crum, Allinger and Steinberg, ibid., 2137.
Le Fèvre and Le Fèvre, Chem. & Ind., 1956, 54.

(38) Brutcher, Roberts, Barr and Pearson, J.A.C.S., 1956, 78, 1441.

(39) Birch and Dean, J.C.S., 1953, 2479.

(40) Godchot, Cauquil and Calas, Compt. rend., 1936, 202, 1129.

(41) Linstead et al., J.A.C.S., 1942, 64, 1985.

(42) Siegel, ibid., 1953, 75, 1317.

(43) Brewster, ibid., 1954, 76, 6361.

(44) Anderson and MacNaughton, ibid., 1942, 64, 1459.
Freidman and Turkevich, ibid., 1952, 74, 1669.

(45) Mozingo, ibid., 1944, 66, 1859.

(46) Winstein and Holness, ibid., 1955, 77, 5562.

(47) Dauben, Blanz, Jui & Micheli, ibid., 1956, 78, 3752.

(48) Vogel, "Practical Organic Chemistry", 1954, 256.

(49) Doering and Aschner, J.A.C.S., 1949, 71, 838.

(50) Vogel, "Practical Organic Chemistry", 1954, 815.

(51) idem., ibid., p. 255.

(52) Umland and Williams, J. Org. Chem., 1956, 21, 1302.

(53) Galinovsky and Vogl, Monatsch, 1948, 79, 325.

ACKNOWLEDGMENTS

My sincere thanks are due to my supervisors Professor J. M. Robertson, F.R.S., and Dr. D. T. Gibson. I am especially grateful to Dr. Gibson for suggesting this research problem, for his constant interest and advice and for his guidance in methods of research. I thank Professor D. H. R. Barton, F.R.S., Dr. J. Bell, Dr. R. I. Reed and Dr. R. P. A. Sneeden for their helpful advice at various stages of this work.

I am indebted to Messrs. Murex and Co. Ltd. for the preparation of special alloys containing platinum; to Dr. O. C. Musgrave for a supply of cholestan-3-one; to Dr. A. Hems of Glaxo Laboratories, Ltd., for samples of methylcyclohexanones; to the Research Department of I.C.I. Ltd., Nobel Division, Stevenston, and in particular the Research Manager, Dr. D. Traill for facilities to complete part of this work; and to the micro-analytical sections at Glasgow University and at Ardeer for micro-analyses.

R. B. B.
